Evaluation of Optical Surface Scanning of Breast Cancer Patients for Improved Radiotherapy

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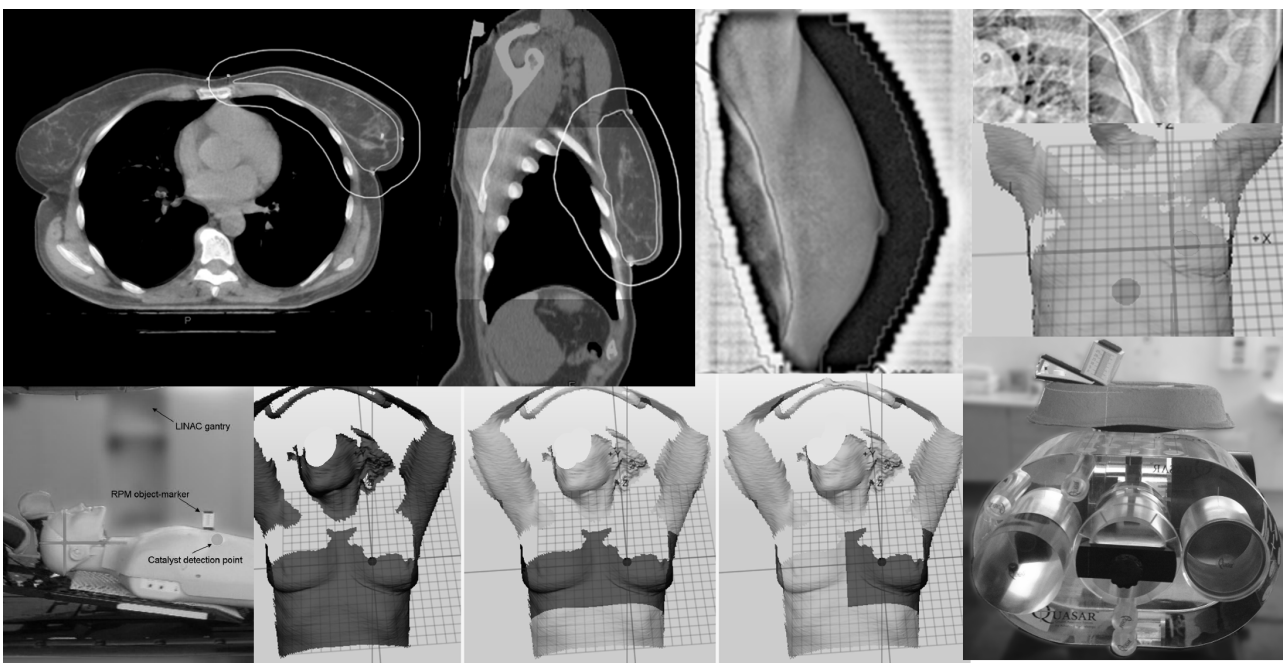

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Preface

This thesis is written in partial fulfilment of the PhD degree requirement at the PhD school of physics at the Technical University of Denmark (DTU). The work was carried out as a collaboration between the Center for Nuclear Technologies (DTU Nutech), the Radiation Physics Division, where I was employed, and the Department of Oncology at Herlev and Gentofte Hospital (HGH), University of Copenhagen.

The project entitled "*Evaluation of optical surface scanning of mammary cancer patients for improved radiotherapy*" was supervised by Claus E. Andersen, Jakob Helt-Hansen, Faisal Mahmood and Claus F. Behrens.

Susanne Nørring Bekke
Risø, January 2018

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Thank you to Wiviann Ottosson for sharing your great knowledge with me and always finding the time to talk; to Patrik Sibolt for your clinical thoroughness and always good mood; to Karen Andersen for always being willing to help; to Malin Kügele and Sofie Ceberg for your great insights and ideas; to Åsa Kronander from C-RAD for your assistance throughout the whole project; to Kurt Nielsen for solving all technical issues; to Sune Kristian Buhl for your invaluable effort through the C-RAD implementation period; to Pia Elhauge for helping me with travel expenses and other paper work, you made everything much easier.

Sincerely thanks to my close family and friends who have been a great support for me during my years as a PhD student. A special thanks to my sister, mother, father and mother-in-law for caring for my home and my children during my absence. To my grandmother Else, who inspired me to do research, and my late grandfather Ole, who taught me the joy of mathematics. To my beautiful children Nanna, Viggo and Lise, thank you for always putting a smile on my face. I would like to dedicate this thesis to my beloved husband Nicolai Nørring Bekke. Thank you for your never-ending encouragement and patience, this work could simply not have been done without you.

Abstract

Patients with breast cancer often receive radiotherapy and it is crucial that the positioning of the patient is reproduced accurately at each treatment fraction. An optical surface scanning (OS) system can automatically and in real-time provide corrections for patient posture and also couch corrections to position the patient as planned, without giving any dose of ionizing radiation to the patient. In addition, the system can monitor the respiratory motion, used for deep-inspiration breath-hold (DIBH) radiotherapy, by tracking a small predefined area on the patient's surface. The objective of the present PhD study was to investigate if OS-systems can lead to improved radiotherapy for breast cancer patients. Potential improvement of radiotherapy was investigated by evaluating (i) the accuracy of the patient setup, (ii) the dose coverage of the target, and (iii) the accuracy of the respiratory motion monitoring. In regard to respiratory motion monitoring, the feasibility of moving the gating area during the treatment course was also investigated.

In a prospective study with 39 left-sided breast cancer patient, the treatment position was evaluated after conventional setup (kilo- and megavoltage X-ray imaging (kV-MV)) for patients with (n = 19) and without (n = 20) arm posture correction using cone beam computed tomography (CBCT) as ground truth. No indications of improved kV-MV based setup with arm posture correction were found. Nonetheless, it was found that the initial patient setup is significantly improved based on surface scans rather than in-room lasers. In a pilot study, involving three out of the 39 patients, it was found that incorrect arm posture led to reduced dose coverage of the target breast. The reduction was however small and based on a limited number of patients.

In a phantom study it was concluded that the OS-system can be used for respiratory motion monitoring. Compared to an alternative external marker-based system, the amplitude estimates from the OS-system are more accurate with no angle-dependency of the patient surface.

In a patient study (n = 194), the feasibility of moving the gating area from an area above the xiphoid process to the target breast was investigated. Based on simultaneous monitoring of the respiratory motion at the xiphoid process and the target breast, it was concluded that the gating area in general should not be moved

Overall it can be concluded that the OS-system can improve radiotherapy for breast cancer patients, as the system can be used for respiratory motion monitoring with more accurate amplitude estimates. The system can also be used for posture corrections where data indicated that arm posture correction can improve dose coverage of the breast. In addition it was concluded, that with the current technology patient setup can not solely be based on OS. Conventional x-ray based imaging of internal anatomy therefore remains an essential part of the clinical workflow. However, the initial patient setup is improved if based on surface scans rather than laser.

Resumé (in Danish)

Patienter med brystkræft behandles ofte med stråleterapi, hvor det er vigtigt, at positioneringen af patienten bliver gengivet nøjagtigt ved hver enkelt behandlingsfraktion. Et optisk overfladeskanningssystem kan automatisk og i *real-time* foreslå korrektioner til patientens positur og leje-position med henblik på at mindske forskellen i lejringen i forhold til den planlagte behandlingsposition. Overfladeskanningssystemet kan desuden registrere vejrtrækningsbevægelser ved at monitorere patientens overflade, hvilket fx bruges til deep-inspiration breath-hold (DIBH) stråleterapi. Formålet med dette ph.d.-studie var at undersøge om et overfladeskanningssystem kan medvirke til at forbedre stråleterapien for patienter med brystkræft. En forbedring af stråleterapien blev undersøgt ved at evaluere (i) nøjagtigheden af patientopstillingen, (ii) dosisdækningen af behandlingsområdet, og (iii) nøjagtigheden af monitoreringen af respirationsbevægelser. I forhold til monitorering af vejtrækningsbevægelser, blev det tillige undersøgt, om det undervejs i behandlingsforløbet er uproblematisk at ændre placeringen af det planlagte måleområde, som registrerer patientens respirationsbevægelser.

I et prospektivt studie med 39 venstresidig brystkræft patienter, blev behandlingspositionen evalueret på CBCT efter patientopstilling var foretaget ved hjælp af røntgenbilleder (et kV billede og et MV feltbillede (kV-MV)). To grupper af patienter indgik, hvor den ene gruppe (n=19) havde fået korrigeret armenes placering ved hjælp af overfladeskanningssystemet inden kV-MV billedtagningen og den anden gruppe (n = 20) ikke havde fået korrigeret armene. Der blev ikke fundet nogen indikationer af, at armkorrektion fører til en forbedret opstilling med kV-MV. Ikke desto mindre, viste data at patientopstilling bliver forbedret med overfladeskanningssystemet, i forhold til en opstilling, der kun er baseret på laser. Data viste dog også, at det er nødvendigt at verificere patientopstillingen med kV-MV billeder. I et mindre pilotstudie, der involverede tre ud af de 39 patienter, blev en reduceret dosisdækning af behandlingsbrystet observeret i forbindelse med forkert placering af armen. Reduktionen var dog lille og baseret på et begrænset antal patienter.

I et fantomstudie blev det konstateret, at overfladeskanningssystemet kan bruges til monitering af vejrtrækningsbevægelser. Sammenlignet med det undersøgte markørbaserede system, var amplitudeestimaterne fra overfladeskanningssystemet mere akkurate idet de ikke blev påvirket af patientoverfladens hældning.

I et patientstudie (n = 194) blev det på baggrund af samtidig monitorering af respirationsbevægelserne ved xiphoid process og ved behandlingsbrystet fundet, at måleområdet generelt ikke bør flyttes under behandlingen.

Samlet set kan det konkluderes, at overfladeskanningssystemet kan forbedre stråleterapi for brystkræftpatienter, da systemet kan bruges til at monitorere vejrtrækningsbevægelserne med mere akkurate amplitudeestimater. Derudover kan systemet bruges til korrektion af patientens positur, hvor data indikerede, at korrektion af armenes placering kan føre til forbedret dosisdækning af behandlingsbrystet. Det blev også konstateret, at med den anvendte teknologi, kan patientopstillingen ikke kun være baseret på overfladeskanningssystemet, og dermed vil røntgenbaseret billedtagning fortsat være en essentiel del af det kliniske workflow.

List of Publications

This thesis is based on the following three papers. The papers are placed in an order relevant for the thesis. The Roman letters (I, II, III) refer to the appendix containing the corresponding paper.

Paper I **Bekke SN**, Mahmood F, and Behrens CF. No indications of improvement in kV-MV based setup using optical surface scanning for arm posture correction in breast radiotherapy. To be submitted.

Paper II **Bekke SL**, Mahmood F, Helt-Hansen J, and Behrens CF. Optical surface scanning for respiratory motion monitoring in radiotherapy: a feasibility study. Proc. SPIE 2014; 9036.

Paper III **Bekke SN**, Kügele M, Behrens CF, Ceberg S, and Mahmood F. Non-interchangeability of gating areas using surface scanning in deep inspiration breath-hold radiotherapy. To be submitted.

Abbreviations

2D	Two-Dimensional
3D	Three-Dimensional
4D	Four-Dimensional
ASR	Age-standardised rate
CBCT	Cone Beam Computed Tomography
CI	Confidence Interval
CRAM	C-RAD mammae
CT	Computed Tomography
CTV	Clinical Target Volume
DBCG	Danish Breast Cancer Coorperative Group
DIBH	Deep inspiration breath-hold
DIR	Deform Image Registration
DTU	Danmarks Tekniske Universitet (Technical University of Denmark)
DVH	Dose Volume Histogram
EPID	Electronic Portal Imaging Device
FB	Free breathing
fx	Fraction
HGH	Herlev and Gentofte Hospital
IGRT	Image Guided Radiotherapy
kV	kilovoltage
Lat	Lateral
LINAC	Linear Accelerator
Lng	Longitudinal
MV	Megavoltage
OAR	Organ At Risk
OBI	On-Board Imager
OS	Optical surface scanning
ROI	Region Of Interest
RPM	Real-time Position Management
RTT	Radiation Therapy Technologist
SD	Standard Deviation
TPS	Treatment Planning System
Vrt	Vertical

Content

Preface iii

Acknowledgements v

Abstract vii

Resumé (in Danish) ix

List of Publications xi

Abbreviations xiii

1 Introduction 1
- 1.1 Breast Cancer . . . 1
- 1.2 Radiotherapy . . . 2
- 1.3 Pre Irradiation Patient Setup Verification . . . 2
- 1.4 Deep Inspiration Breath-hold (DIBH) . . . 4
- 1.5 Uncertainties Related to Breast Radiotherapy . . . 5
- 1.6 Optical Surface Scanning System . . . 8

2 Objectives 15

3 Materials and Methods 17
- 3.1 CRAM Protocol . . . 17
- 3.2 C-RAD OS-systems at HGH . . . 18

4 Overview of Results and Discussion 25
- 4.1 Pre Irradiation Patient Setup Verification (Paper I) . . . 25
- 4.2 Respiratory Motion Monitoring(Paper II and III) . . . 28
- 4.3 Post Irradiation Dose Verification (Pilot Study) . . . 31

5 Conclusion 35

5.1 Future perspectives 36

Bibliography 37

Appendices 45

Appendix A Dosimetric Effect of Arm Posture Variation (Pilot Study) 47

Appendix B CRAM Protocol (in Danish) 63
B.1 Protocol 63
B.2 Information for Patients 70
B.3 Treatment Guidelines 75
B.4 Treatment Schedule Handout 102

Papers 109

Paper I Setup With and Without Arm Posture Correction 111

Paper II Respiratory Motion Monitoring in Radiotherapy 135

Paper III Non-Interchangeability of Gating Areas 145

CHAPTER 1

Introduction

1.1 Breast Cancer

One out of 10 women in Denmark develops breast cancer and it is the most common form of cancer in women with 4686 new cases diagnosed per year (average over 2010-2014), representing 25.7 % of all new cancer cases [1]. The incidence has increased with a peak around 2009 caused by the introduction of a national screening program in Denmark from 2008 for women aged 50-69 (Figure 1.1). The breast cancer-specific mortality rate has decreased since mid-1990s, which may be explained by earlier diagnosis and improved treatment strategies [2]. The five-year survival rate was 86 % based on the years 2010-2014.

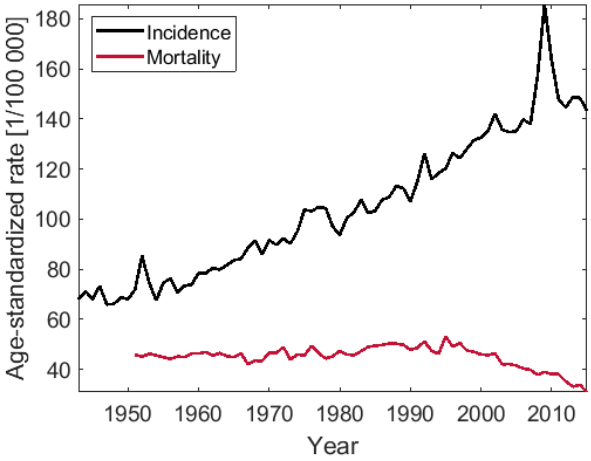

Figure 1.1: Age-standardised rate (ASR) per 100,000 women in Denmark. ASR is a weighted average of the age specific rate. The weighting is here based on the age distribution in Nordic countries. Data from NORDCAN [1].

1.2 Radiotherapy

The primary treatment for breast cancer is surgical removal of the breast (mastectomy) or breast-conserving surgery (lumpectomy). In Denmark more than 70 % of the patients with invasive breast cancer underwent lumpectomy in 2016 [3]. Radiotherapy, and/or systemic therapy (chemotherapy, endocrine therapy, trastuzumab) may be offered as adjuvant therapy. Radiotherapy is used to reduce the risk of both local cancer recurrence and breast cancer death [4], by delivering high dose to the target (whole breast, post-mastectomy chest-wall, axillary, internal mammary and supraclavicular lymph nodes) while minimizing the dose to the organs at risk (OARs, heart, lungs, contralateral breast). In Denmark the Danish Breast Cancer Coorperative Group (DBCG) provides evidence-based guidelines for diagnosis and treatment of breast cancer. In concordance, mammary cancer patients in Denmark eligible for curative-intent radiotherapy, often receive 25 fractions of radiotherapy administered as one fraction per day, 5 days a week (50 Gy/25 fractions). Hypofractionation based on 40 Gy/15 fractions is offered for patients after lumpectomy without lymph node involvement [5]. In some cases patients are after lumpectomy (< 50 years or narrow negativ margin) offered a boost to the cavity (tumour bed) based on 10 Gy/5 fractions or 16 Gy/8 fractions to reduce the risk of local recurrence [6, 7]. The lumpectomy cavity can be identified using 4–8 clips inserted during lumpectomy.

The treatment planning is based on a computed tomography (CT) scan of the patient acquired some days before the first treatment fraction. In treatment planning it is assumed that the CT image represents the patient geometry at all treatment fractions. Thus it is crucial that the patient geometry is reproduced accurately at each treatment fraction. Hence, efforts are put into positioning the patient in the same way during treatment as during the CT scan used for treatment planning.

Traditionally, the initial setup is done by positioning the patient on a special breast board with support for arms and head followed by alignment guided by tattoo marks and in-room lasers (laser based setup). However these external marks are often not an accurate representation of the target position, and hence setup verification using image guided radiotherapy (IGRT) can be used to ensure the position.

1.3 Pre Irradiation Patient Setup Verification

Before treatment delivery the patient setup can be verified using different imaging modalities, and corrected accordingly to increase the accuracy of the radiotherapy. IGRT can reduce the setup uncertainties (or errors) and potentially be used to reduce the margins that are added to the clinical target volume (CTV) to account for any systematic and random errors [8] (defined in section 1.5). Examples of setup verification includes planar megavoltage (MV) field imaging, planar kilovoltage (kV) imaging, cone beam computed tomography (CBCT) and setup using optical surface scanning (OS, surface based setup).

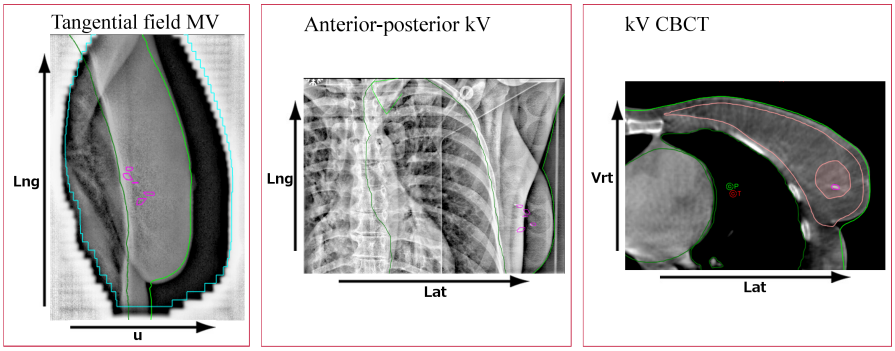

Figure 1.2: Different setup verification images. The images are registered to the planning CT and structures from planning CT are visualised. Clips are visible on kV images. The **u** direction is a linear combination of the lateral ($\approx$ 1/3) and vertical ($\approx$ 2/3) direction. Images from patient 12 fraction 2 from CRAM protocol (Described in section 3.1).

Field imaging is the most widespread technique and can be generated using portal film or using an electronic portal imaging device (EPID). Field imaging allows visualization of the multileaf collimator positions together with the patient anatomy (Figure 1.2), and can also be acquired in real-time during treatment delivery without additional imaging dose [9]. Using a gantry-mounted kV imaging system, planar kV images can be acquired with improved bone/soft tissue contrast compared to MV imaging. This system can in addition to the traditional radiographic images also acquire real-time fluoroscopic images for monitoring of e.g. breathing motion [9]. The system can also be used to acquire kV CBCT where full three-dimensional (3D) information is achieved with bone/soft tissue contrast and is hence often used as the ground truth for evaluation of setup errors. A larger portion of the body is irradiated with kV CBCT compared to tangential MV imaging, and the mean dose to the healthy surrounding organs as the heart, and contralateral breast and lungs are larger, while the mean target dose is higher for MV imaging [10]. The acquisition of CBCT is significantly longer ($\approx$60 s for low dose thorax protocol) compared to planar imaging techniques.

Surface based setup using an OS-system does not use ionising radiation and is based on the correspondence between the surface of the patient and the target position. Such OS-systems can provide corrections for patient posture, e.g. arm posture, which is not easy to correct for with planar images, and also automaticly provide couch adjustments in six degrees of freedom to move the patient to the planned treatment position. In addition the system can be used to monitor the respiratory motion and patient movement during treatment delivery. The OS-systems have shown to be more accurate than laser based setup [11–13], and have shown potential to reduce the number of days with need for position verification using imaging based on ionizing radiation [14–16]. More on the

OS-system in section 1.6.

1.4 Deep Inspiration Breath-hold (DIBH)

In left-sided breast cancer especially, the use of radiotherapy induces an increased risk of cardiac mortality [17]. The rate of ischemic heart disease has been found to be proportional to the mean dose to the heart [18]. Much effort has been done to reduce the radiation dose to the heart, for example by optimization of dose plans. One other method is a motion management technique called deep inspiration breath-hold (DIBH). With DIBH, patients are (using audial guidance with or without visual feedback), asked to take a deep breath and hold it during irradiation. When the lungs are inflated the distance between the target (breast and lymph nodes) and heart is increased [19, 20] and a lower fraction of the lung volume is irradiated [21]. Several studies have shown that irradiation during DIBH leads to significantly reduced dose to the heart and lungs compared to irradiation during free breathing (FB) [22–26]. Studies have also shown that visual guidance for the patient can increase the stability of the breath-hold throughout treatment [27, 28]. Visual guidance requires monitoring of the respiration motion. One system widely used to monitor the respiratory motion for breast cancer patients is the Real-time Position Management (RPM) system (Varian Medical Systems, Palo Alto, CA) which is based on tracking of a physical marker placed on the patient's skin close to the target area [29–31]. An alternative method uses an OS-system to track the patient's surface directly without the use of an object-marker, and enables acquisition of surface data within a selected area in real-time [9, 32–35]. Such systems are commercially offered by C-RAD (C-RAD Positioning AB, Uppsala, Sweden) and VisionRT (London, UK). Respiratory motion monitoring using C-RAD, VisionRT and RPM is illustrated in Figure 1.3.

With the OS-system offered from C-RAD it is possible to track the respiratory motion in the vertical direction using two different spatial areas simultaneously, however only one of the signals is used to automatically trigger imaging and treatment. In addition to this the whole surface can be used to monitor the patient during treatment (patient monitoring) and in real-time give couch adjustments in six degrees of freedom to move the patient to the planned treatment position [34]. This is done by matching the live surface with a daily DIBH surface reference using a non-rigid registration algorithm (described in subsection 1.6.2). The daily DIBH surface reference is captured for each treatment session during the first breath-hold, for example in connection with planar MV or kV imaging. If the length of the error vector (calculated from the lateral, longitudinal and vertical error) or a posture error is above a specified tolerance the beam will automatically be turned off. The information from patient monitoring is not used for the patient's visual guidance, this will only be respiratory motion signal collected within the gating area.

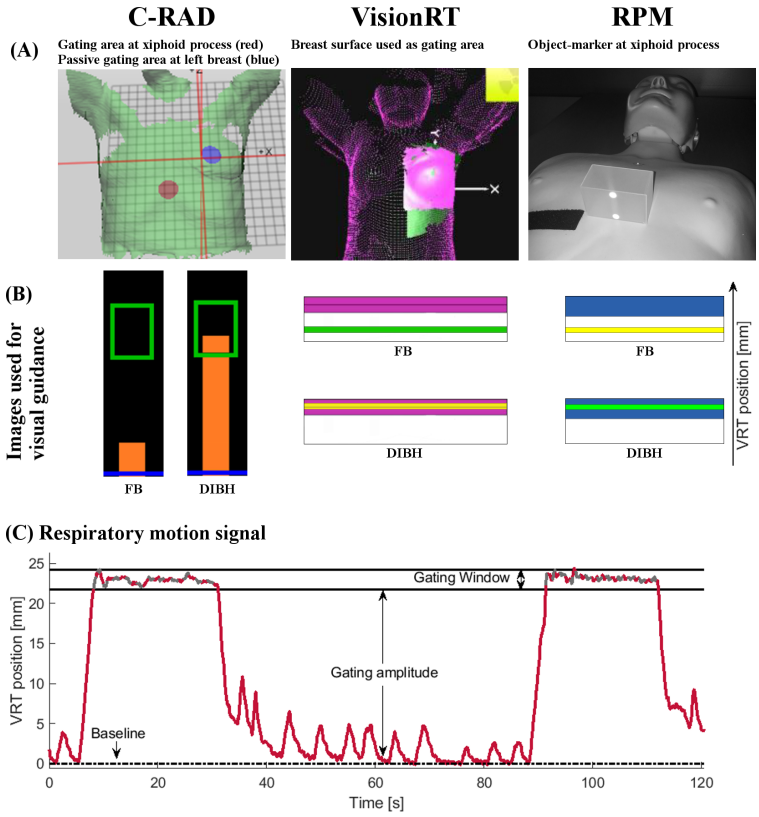

Figure 1.3: Methods for monitoring the respiration motion of breast cancer patients. (A) The respiratory motion is tracked using a selected surface area (C-RAD and VisionRT) or an object-marker (RPM). (B): The images presented to the patient for visual guidance. (C) Example of the respiratory motion signal (red). Some images are edited from VisionRT.

1.5 Uncertainties Related to Breast Radiotherapy

Variation in target position can occur from day to day (inter-fraction) caused by uncertainty in patient setup, weight loss/gain or swelling of the breast, or occur during a treatment fraction (intra-fraction) due to e.g. breathing motion and/or patient sliding down the breast board. Errors caused by the variation in target position are usually divided into systematic and random errors. Systematic errors (strongly correlated) are similar from day to day and can be caused by delineation errors, calibrations errors (e.g. in-room lasers) and patient or organ motion at CT [36]. Random errors (weakly correlated) vary from day to day and include target motion and day-to-day variation in patient setup or equipment. The

systematic and random errors can be quantified using the mean (μ) and standard deviation (SD). Another approach is to evaluate the two types of errors using the group mean (M), the SD of the systematic error (Σ) and the SD of the random error (σ) [8]. M is the mean of all individual patient means. Σ is the SD of all individual patient means and describes how reproducible the treatment preparation is done. σ is the root mean square of the SD from each individual patient, and reflects the magnitude of the day-to-day setup variation.

Table 1.1 gives a representative overview of inter-fraction errors based on setup using laser, kV and MV imaging. From the table it can for example be seen that typically the mean (μ) or group mean (M) is below 1 mm for setup based on kV or MV imaging, while these for laser based setup can be as high as 3.4 mm. The systematic (Σ) and random (σ) errors are in general higher for a laser based setup, and in addition the percentage of setup errors with a length <5 mm is lower. The studies by Lutz et al. and Thomsen et al. included in Table 1.1, were performed at the same institution, using the same technique but performed during DIBH and FB, respectively [30, 37]. The reported systematic and random inter-fraction errors were similar, and hence they concluded that the main advantage of DIBH is found in the increased distance between the target and heart during breath-hold. Studies have shown that inter-fraction target motion in general is larger than intra-fraction motion. [38–40]. Kron et al. measured the mean intra- and inter-fraction variability of the central lung distance on field images to 1.06 $\pm$ 1.19 mm (1 SD) and 1.82 $\pm$ 0.59 mm, respectively [39]. The target motion during FB was evaluated by Glide-Hurst et al., using four-dimensional (4D) CT together with deformable image registration (DIR), they measured the mean 3D vector motion of the lumpectomy cavity and target breast during a FB cycle to 2.5 $\pm$ 1.0 (1 SD) and 2.0 $\pm$ 0.8, with negligible motion in the lateral direction [41].

Table 1.1: Inter-fraction setup errors for patients with breast cancer evaluated using different methods (ground truths).

Author	Year	pts	Ground truth	Setup	Breath method	Direction	μ	SD	M	Σ	σ	|max|	<5 mm
							[mm]						[%]
Bekke et al. Paper I	-	39	CBCT	Laser	DIBH	Lat	1.5	3.9				13	74
					(surface)	Lng	-0.9	4.0				13	78
						Vrt	-1.5	4.9				15	78
						|Δ|	6.5†					18	
				AP kV and		Lat	-0.4	2.6				7	91
				tangential MV		Lng	0.9	3.0				8	85
						Vrt	-0.2	3.4				15	84
						|Δ|	4.2†					16	
Lawson et al. [42]	2008	25	Orthogonal kV-kV	Laser	FB	Lat	1.0		1.4	3.1	5.2	22	77
						Lng	-0.8		-0.9	3.7	4.8	42	66
						Vrt	0.5		0.6	4.1	4.2	20	78
						|Δ|	7.3†					45	
Mülliez et al. [43]	2016	103	CBCT	Laser, some with	FB	Lat				2.7	3.6		
				offline correction		Lng				2.8	3.4		
				strategy		Vrt				3.1	3.8		
Alderliesten et al. [44]	2013	20	CBCT (surface)	Surface	DIBH	Lat			0.8	1.7	1.3	≈ 10	
					(no visual guidance)	Lng			-0.1	1.5	1.5	≈ 8	
						Vrt			-1.5	1.5	1.2	≈ 8	
Bartlett et al. [45]	2013	23	CBCT	Laser	DIBH	Lat			0.5	2.5	2.4		
					(in-room lasers+)	Lng			3.4	3.9	4.1		
						Vrt			0.3	2.8	2.7		
			MV-MV			**u**			-0.2	1.8	2.1		
Conroy et al. [46]	2016	42	Continuous MV	Laser, and AP and	DIBH	**u**			0.4	3.0	2.6	≈ 11	80.8
				tangential MV	(in-room lasers+)								
Lutz et al. [30]	2015	58	Continuous MV	Orthogonal	DIBH	**u**			-0.1	1.4	1.7	16	98
				kV-MV	(object marker)								
Thomsen et al. [37]	2014	16	Continuous MV	Orthogonal	FB	**u**			0.7	1.5	1.1	6	98-99*
				kV-MV									

pts: number of patients. Max: maximum. Lat: lateral. Lng: longitudinal. Vrt: vertical. |Δ|: length of error vector (calculated from lat, lng and vrt error). AP: Anterior-posterior. *Reported as ≤5 mm (not <5 mm). +DIBH was visually monitored using in-room. †Reported as median.
The **u** direction is a linear combination of the lateral (≈ 1/3) and vertical (≈ 2/3) direction. The paper from Bekke et al. will be discussed in Section 4.1.

1.6 Optical Surface Scanning System

In the following subsections the OS-systems from C-RAD, installed at Herlev and Gentofte Hospital (HGH), will be described and the main differences between these and a alternative commercial system (AlignRT) will be highlighted. An example of a C-RAD installation at HGH can be seen in Figure 1.4.

Figure 1.4: The Catalyst HD system from C-RAD with three cameras installed in the ceiling of on of the treatment rooms at HGH. Catalyst only consists of the central camera in front of the gantry.

1.6.1 Surface Imaging

Different OS-systems used for positioning and monitoring without the use of markers has been developed over the last years and can be divided by the technique they are based on: active or passive triangulation or time-of-flight [47, 48]. With active triangulation the 3D surface is derived using the geometry between a light source, target (patient) and camera, while passive triangulation uses the geometry between two cameras (stereo) and the target. With passive triangulation a light source, for example a projected speckle pattern, can be added to overcome problems associated with texture less surfaces [49]. Time-of-flight on the other hand uses the speed of light together with the phase shift between the emitted light signal and light signal reflected by the target. The main commercial systems offered is AlignRT [50, 51] (from VisionRT) based on passive triangulation with speckle pattern projection and, Catalyst [51, 52] and Sentinel [53, 54] (both from C-RAD) based on active triangulation (Table 1.2). Catalyst and AlignRT captures the whole surface in

one acquisition, while the laser based system Sentinel (635-690 nm) instead scans in steps along the longitudinal direction. Consequently the acquisition time for Sentinel is longer compared to Catalyst and AlignRT. With Catalyst the light source is a sequence of structured near-visible light (405 nm) patterns that are projected onto the patient. The distorted light patterns is imaged by one (Catalyst) or three cameras (Catalyst HD), and the 3D surface can be extracted from these images [55, 56] (Figure 1.5).

Table 1.2: Characteristics of the OS-systems from C-RAD and VisionRT. Data provided by C-RAD and VisionRT, and from [44, 57–59].

Vendor	**C-RAD**			**VisionRT**
Model	**Catalyst**	**Catalyst HD**	**Sentinel**	**AlignRT**
Installed in	Treatment room	Treatment room	CT room	Treatment room
Number of cameras	1	3	1	2-3
Max 3D surfaces per second	16	14	1	5
Positioning accuracy [mm] (rigid body only)	< 1	< 0.5	-	< 1
Number of active references	1	1	1	Multiple
Registration algorithm	Non-rigid	Non-rigid	Non-rigid	Rigid
Visual guidance area	Circular area*	Circular area*	Circular area*	Often whole breast is used
Automatic beam-hold	Varian, Elekta	Varian, Elekta	-	Varian, Elekta
Automatic couch control	Varian	Varian	-	Varian
Daily calibration	In-room lasers	In-room lasers or kV-MV	In-room lasers	In-room lasers or kV-MV
Imaging principle	Active triangulation	Active triangulation	Active triangulation	Passive (stereo) triangulation
Breathing handling	Surface averaging+	Surface averaging+	-	Gated capture, e.g. at end expiration
Posture correction	Color map projection	Color map projection	-	On screen†

*Often placed near xiphoid process with a 2 cm radius. +Surface averaging over a set time period, e.g. 5 s. †VisionRT uses a rigid registration algorithm and posture errors are therefore corrected by visual inspection of the reference and live surface on-screen.

1.6.2 Surface Registration

The OS-system is capable of detecting deviations between a current surface (live surface) and an earlier recorded reference surface. By comparing these surfaces, the system can provide corrections for patient posture, and couch adjustments in six degrees of freedom to move the patient to the planned treatment position. In the current subsection, the algorithm behind surface alignment using the Catalyst (also valid for Catalyst HD) system will be described, as this is the system used throughout the study for the surface based setup. Surface based setup using the Catalyst system is firstly done by correcting any posture errors, followed by any couch corrections. With Catalyst, posture errors are calculated in less than 0.5 seconds and a colour map is projected on the skin of the patient.

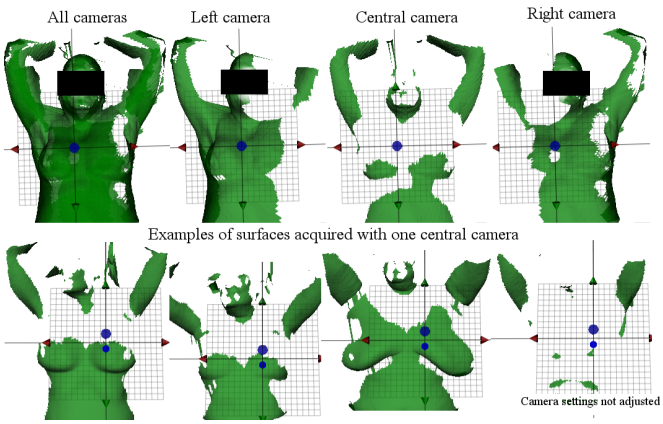

Figure 1.5: Surface scans from the single-camera (Catalyst) and three-camera (Catalyst HD) solution from C-RAD. Top row: the surface generated from all three cameras and each individual camera. With Catalyst, the central camera is used to generate the surface. Bottom row: Typical surface scans generated by the Catalyst, and an example of a surface acquired with (very) poor camera settings.

The calculation of the posture errors are based on a vector from a point on the reference surface and a corresponding point on the live surface. The length and direction of this vector is used to create the colour map. No colour is projected if the vector length is within a certain tolerance (5 mm surface tolerance was used in Paper I) while the colour (yellow/red) identifies the direction of the posture correction (Figure 1.6). Any couch correction is not included in the posture errors, and hence it is presented separately in order to move the patient to the planned treatment position.

The calculation of the couch corrections can be divided into two main steps 1) a non-rigid registration algorithm that aligns the reference surface to the live surface and 2) a volumetric non-rigid model that predicts the influence on the estimated isocenter position (the planned isocenter position within the patient) using the results from step 1. Both steps are company secrets but the principles behind each of them can be found in the papers by Li et al. and Summer et al. [60–62] (step 1), and Nutti et al. and Müller et al. [52, 63] (step 2). In the non-rigid registration algorithm (step 1) a corresponding point on the live surface is found for each point on the reference surface (Figure 1.7). The registration is based on an iterative process that initially favours global rigid alignment and subsequently lowers the stiffness of the object in order to detect local deformations (posture errors).

When the reference surface is aligned to the live surface, the vector field describing the displacement of each point on the reference surface can be used to calculate the estimated isocenter position. A volumetric mesh consisting of uniformly distributed

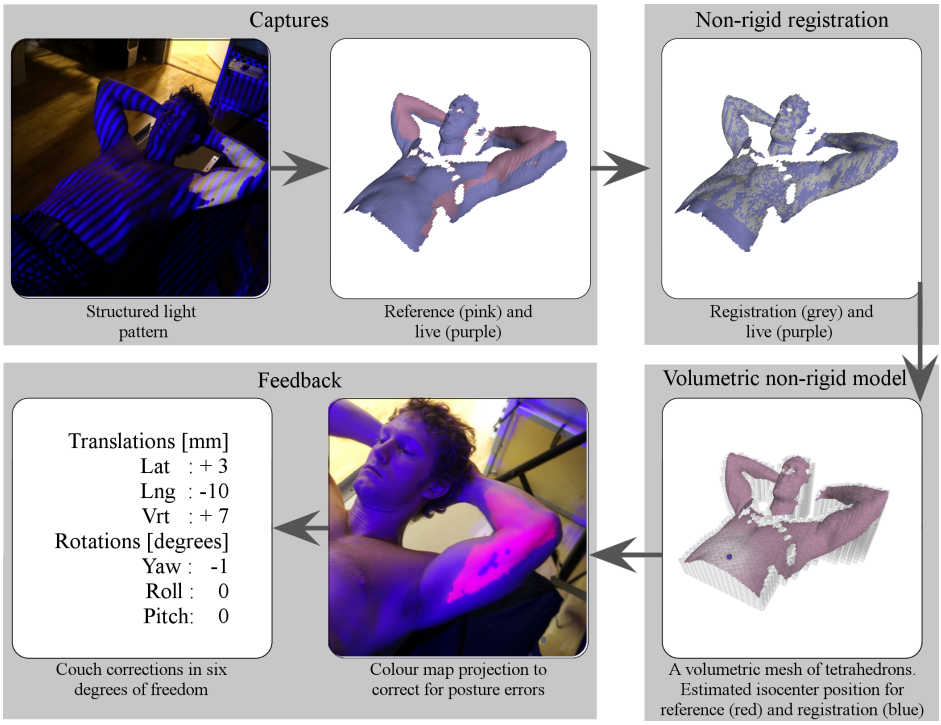

Figure 1.6: The Catalyst workflow for surface based setup. A live surface is captured and aligned with the reference surface. The allignment is used to predict the influence on the estimated isocenter position. The results are provided as posture and couch corrections. Figure edited from Nütti et al. [52].

tetrahedrons are created in order to encapsulate all triangles from the reference surface mesh (Figure 1.6). The displacement of a specific node in the volumetric mesh, for example the node representing the planned isocenter position, depends on the vector field found from the non-rigid registration. The influence of each vector decreases with the distance to the specific node. For this reason a difference in arm posture has lower impact on a node within the breast, than a difference in breast posture would have.

1.6.3 Surface Reference

The reference used for the surface based setup can be acquired with the OS-system in the CT or treatment room, or alternatively be derived from the planning CT. Based on previous studies the reference derived from the planning CT tends be the preferred choice, as an OS-system is often not available in the CT room [16, 50, 64]. A previous study have

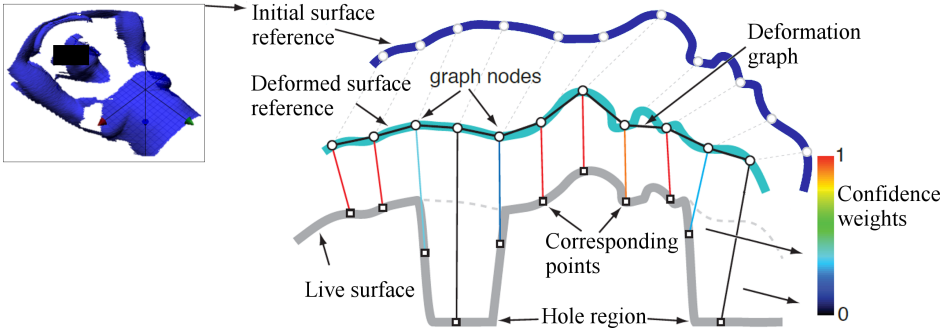

Figure 1.7: An example of a surface reference (blue) together with an illustration of the non-rigid registration algorithm. The algorithm solves for the transformations of each graph node, the corresponding points on the live surface, and the confidence weights. Graph nodes are created by uniform sampling of the surfaces. Some reference surface points do not have a corresponding position on the live surface (hole regions). In these cases the correspondence is zero-weighted (black) and do not influence the deformation. Edited from Li et al. [60].

noted that a reference acquired with an OS-system in the CT room would be preferred to avoid any systematic error [16]. The CT is acquired over a longer period (≈15 s) and breathing artefacts in the form of "rippling" can be observed [14, 65], in addition it is thought that using the same imaging technology for the reference surface could be preferable. A reference acquired in the CT room does however require a coordinate system change (CT to treatment room), which can induce a systematic setup error. A surface reference from the first treatment fraction is susceptible to the introduction of any systematic error for subsequent fractions, which might be avoided by using an offline strategy, e.g. no action level protocol [66]. Table 1.3 gives a summary of publications on surface based setup, and it can be seen that; the surface derived from the CT scan is primarily chosen as surface reference; there is a tendency towards a larger standard deviation (SD) of the setup errors in the longitudinal direction; the mean setup error (μ) is in the range -2 to 2 mm in the lateral direction for all studies, while it exceeds this range for two studies in the longitudinal and two studies in the vertical direction.

Table 1.3: Summary of publications on surface based setup for patients with breast cancer or intra-thoracic tumours.

Author	Year	System	pts	Site	ROI	Ground truth	Breath method	Ref.	Trans. error μ(SD) [mm]				Rot. error μ(SD) [deg]		
									|Δ|	Δ_{lat}	Δ_{lng}	Δ_{vrt}	Δ_{yaw}	Δ_{roll}	Δ_{pitch}
Bekke et al. Paper I	-	Catalyst	39	Br.	Both Br.‡	CBCT	DIBH	Surf(CT)	5.8†	–0.1(3.0)	–1.9(4.0)	0.5(4.1)	0.2(1.4)	–0.5(1.6)	0.9(1.8)
					Both Br.				6.2†	–0.5(3.1)	–2.3(4.1)	0.8(4.2)	0.1(1.4)	–0.7(1.5)	1.2(1.8)
					Br				6.2†	–0.8(3.6)	–2.2(4.2)	0.8(4.2)	–0.2(2.2)	–0.8(1.8)	1.0(1.7)
Stanley et al. [13]	2017	Catalyst HD	≈ 600 fx	Br.	-	CBCT	FB	CT	6(2)						
Walter et al. [67]	2016	Catalyst	8	Tho.	Both Br.‡	CBCT	FB	CT		0.6(2.6)	–5.0(7.9)	0.5(3.2)			
Pallotta et al. [11]	2015	Sentinel	10	Tho..	-	CBCT	FB	CT		–0.3(2.7)	0.0(3.8)	–1.3(2.7)	0.3(1.2)	–0.3(1.2)	0.1(1.2)
Stieler et al. [15]	2013	Catalyst	5	Tho.	-	CBCT	FB	CT		0.7(3.3)	–0.7(3.8)	2.4(3.2)	0.7(1.5)	–0.6(1.9)	–0.3(1.8)
Pallotta et al. [68]	2013	Sentinel	19	Tho.	-	CBCT	FB	**CT**		–0.4(2.0)	–1.7(3.2)	–1.6(1.8)	0.2(1.2)	–0.1(1.2)	0.0(1.1)
								Surf		–0.8(1.7)	–0.2(3.3)	0.1(1.8)	–0.4(1.5)	0.4(1.1)	0.5(1.0)
Stieler et al. [54]	2012	Sentinel	<21	Tho.	-	CBCT	FB	CT		–1.3(3.6)	0.9(5.2)	0.8(4.3)	0.6(1.4)	0.1(0.9)	0.3(1.0)
Moser et al. [14]	2013	Galaxy+	20	Br.	-	MVCT	FB	CT	10.1†	0.2†	2.0†	–8.7†		–0.2†	
								Surf	5.4†	–0.1†	–0.5†	–2.3†		–0.1†	
Gierga et al. [65]	2008	AlignRT	12	Br.	Br.	kV-kV (clips)	FB	CT	4.9†						
			4				FB	Surf	6.2†						
			8				FB (exp)	**Surf**	3.2†						
									Comment						
Crop et al. [69]	2016	Catalyst	95	Br.	Both Br.‡	MVCT	FB	CT	Same result despite choice of surface reference (CT/surf).						
								Surf	Surface based setup performs equaly to MVCT based setup based. Surface based setup performs significantly better than laser based setup.						
Shah et al. [12]	2013	AlignRT	50	Br.	Br.	MV	FB (exp)		Surface based setup error $\leq$ 3 mm in any direction for 86 % of the fractions.						
Alderliesten et al. [44]	2013	AlignRT	20	Br.	Both Br. Br.	CBCT	DIBH	CT	OS is suitable for monitoring DIBH for left-sided breast cancer. Do not recommend solely the use of the OS-system for setup verification and monitoring.						
Deantonio et al. [16]	2011	AlignRT	15	Br.	-	MV	FB	Surf	Surface based setup might reduce fractions with need for MV imaging.						

pts: number of patients. Ref: surface reference. |Δ|: error vector (derived from translational errors). μ: mean. SD: 1 standard deviation. Br.: breast. Tho.: thoracic. fx:fraction. exp: end expiration. Surf(CT): Surface acquired using OS-system in CT room. Surf: surface acquired at first fraction. CW: chest-wall. Bold Surf or CT indicates that this choice of reference was found to give more accurate results. ‡Reference surface includes more than just the two breasts. †reported as median and not mean. +distributed by LAP Laser, Germany, but originally developed by C-RAD, Uppsala, Sweden; it was further developed under the name Sentinel.

CHAPTER 2

Objectives

The present thesis covers measurements performed at Herlev and Gentofte Hospital (HGH) using the optical surface scanning (OS) systems from C-RAD installed at eight linear accelerators (LINACs) and two CT scanners. The objective for the present PhD was to investigate if the OS-systems can lead to improved radiotherapy for breast cancer patients. Improved radiotherapy was evaluated primarily regarding the positioning accuracy of the patient setup and the accuracy of the respiratory motion monitoring, and also partly regarding dose coverage of the target. The main potential benefits of the OS-system in comparison to the conventional patient setup technique at HGH is that the system, based on surface scans, automatically and in real-time can provide corrections for both patient posture and couch corrections in six degrees of freedom to position the patient as planned, without giving any dose of ionizing radiation to the patient. Through the different investigations answers to the following questions were sought:

1. Can patient setup using the OS-system make the conventional patient setup technique, based on ionizing radiation, redundant?
2. Can arm posture correction using the OS-system improve the conventional patient setup technique?
3. Can arm posture correction using the OS-system improve dose coverage of the target
4. Can rotation setup errors be reduced with the OS-system?

In addition the following were evaluated regarding respiratory motion monitoring used for deep inspiration breath-hold (DIBH) radiotherapy:

5. Can the respiratory motion be monitored with an OS-system as an alternative to an external marker-based system with similar accuracy?

The investigations were carried out in the period from April 2013 to April 2017 and the research can be divided into the following studies:

Prospective Clinical Trial – Dosimetric and Positional (setup) Effects of Arm Posture Correction
A total of 39 patients with breast cancer treated with DIBH radiotherapy after lumpectomy were enrolled to the C-RAD mammae (CRAM) protocol, approved by the Copenhagen Regional Committee on Health Research Ethics. This involved arm and head posture corrections with the OS-system for 19 patients, and in addition to the conventional patient setup technique (planar kV image and MV field image (kV-MV)) at HGH, it involved daily surface scans and weekly kV CBCT. The collected data were used to investigate if arm posture correction using the OS-system can lead to improvement in the current kV-MV technique with CBCT as ground truth (Paper I) or to improved dose coverage of the target (Pilot study, Appendix A). In addition the potential treatment position based on a surface based setup was compared to the setup based on a laser and based on kV-MV, using the kV-MV or CBCT as ground truth (Paper I).

Phantom Study – Accuracy of Respiratory Motion Monitoring
Measurements performed with two moving phantoms simulating sinusoidal breathing were used to evaluate the accuracy of the respiratory motion monitoring of the OS-system compared to an external marker-based system (Paper II).

Patient Study – Interchangeability of Gating Areas
A total of 262 left-sided breast cancer patients treated with DIBH radiotherapy after lumpectomy or mastectomy were analysed in the present study. The respiratory motion was monitored at two spatial surface areas (2 cm radius) simultaneously for 194 lumpectomy patients. The collected patient data was used to investigate the feasibility of spatially moving the gating area during the treatment course; in addition, the inter-fraction baseline variation was investigated for both patient groups (Paper III).

CHAPTER 3

Materials and Methods

Materials and methods of this PhD thesis are presented in the individual papers while the pilot study on the dosimetric effect of arm posture variation is included in Appendix A. Further details on the CRAM protocol and the use of the OS-system in connection with the different studies, are gathered in the next sections.

3.1 CRAM Protocol

A total of 39 breast cancer patients treated with DIBH radiotherapy after lumpectomy were enrolled to the C-RAD mammae (CRAM) protocol from February 2016 to April 2017 (Table 3.1). All included patients gave informed consent to participate in the protocol approved by the Copenhagen Regional Committee on Health Research Ethics (No. H-15010813).

The specific inclusion criteria were left-sided breast cancer patients without lymph node involvement scheduled for DIBH radiotherapy; however only lumpectomy patients were enrolled as mastectomy patients without lymph node involvement is rarely encountered at HGH. Patients without lymph node involvement were chosen as the main part of the lymph node region was outside the field of view of the CBCT scan, in order to encompass as much as possible of the CTV (scan volume is limited to 16 cm in the longitudinal direction). Another group in Lund had already shown promising results (all though not published) on surface based setup for breast cancer patients in free breathing using the same OS-system [70] (study described later in section 4.1).

More details on the protocol can be acquired in Paper I and Appendix B (the latter in Danish).

3.2 C-RAD OS-systems at HGH

The OS-systems from C-RAD replaced the RPM system for respiratory motion monitoring in June 2014 at HGH. The system has been used for surface based setup as part of the CRAM protocol, but this is not yet a part of the clinical setting at HGH. The single-camera solutions Catalyst, installed at eight LINACs (Varian Clinac iX 2300, Medical Systems, Palo Alto, CA) and Sentinel, installed at two CT scanners (16 slice Philips Brilliance CT Big Bore scanner, Philips Medical Systems, Cleveland, OH) were used throughout the different studies (Table 3.2).

3.2.1 Quality Assurance

At HGH the OS-system is calibrated daily in the CT rooms and three times a week in the treatment rooms using the in-room lasers. The calibration procedure is performed by placing a dedicated phantom on the treatment couch using the in-room lasers (Figure 3.1A). Subsequently a surface scan is acquired, and the deviation relative to the last calibration, will be presented together with the deviation relative to the last isocenter adjustment, and if needed any deviations are compensated for. The isocenter is determined for the OS-system during the initial installation, but can also be adjusted later on if needed. At HGH quality assurance insures that the difference between the isocenter of the in-room lasers and the LINAC or CT is within 2 mm. As a consequence, a systematic error up to 2 mm can potentially be introduced from both the CT room and treatment room. In addition a random error can occur if the patient at one fraction is moved from one treatment room to another.

The uncertainty from the lasers can be avoided using a calibration procedure with a second phantom (QUASAR Penta-Guide, Modus Medical Devices Inc., London Canada), which is designed for calibration to the treatment isocenter and the imaging isocenter (Figure 3.1B). This calibration method is offered for the Catalyst HD systems (installed in late 2016) but is not a part of the clinical setting at HGH.

A phantom based on an manikin, in-house altered to simulate sinusoidal motion, was developed in regard to Paper II. The phantom is not used directly for quality assurance, but is frequently used for educational purposes regarding the OS-system (Figure 3.1C).

3.2.2 OS Camera Settings

As part of the CRAM protocol the OS camera settings was optimized if the surface quality was poor. The parameters to be set were threshold value (Sentinel specific), gain (Catalyst specific) and integration time. The threshold value is the camera sensor limit, which must be exceeded for a pixel to be part of the image; the standard value is 400. The gain parameter is an amplifier; the standard value is 400 %. Integration time or exposure time is the time of light absorption and is dependent on skin type; standard values are in the range of 1500-6000 μs. A very high integration time will naturally lead to a slower

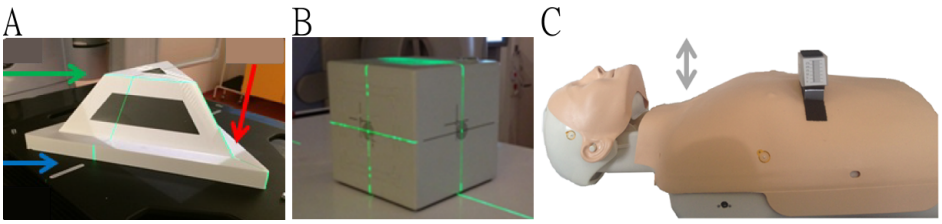

Figure 3.1: Different OS phantoms. A: The phantom used for calibration to in-room lasers. B: The phantom used for calibration to the treatment isocenter and the imaging isocenter. C: Phantom developed for use in Paper II.

update rate of the 3D surface images. High camera sensitivity means a higher value of the camera integration time, and is warranted for a dark skin tone. Too low integration time can lead to underexposure while too high integration time can lead to overexposure (Figure 3.2). In general it is advisable to use the general camera settings that is specific to the individual rooms room (low, medium and high sensitivity), by doing this a manual change of camera settings can be avoided when going from the CT room to a treatment room, or from one treatment room to another. But if the general settings are not suitable they should be optimized to the skin of each individual patient. In one case in the CRAM protocol, the camera settings were not adjusted (example in Figure 1.5 page 10) even though the surface quality was very poor, and consequently data from this fraction was excluded.

3.2.3 Correction for CT marker movement from FB to DIBH

At HGH the patients receiving DIBH radiotherapy are initially setup in FB in both the CT room and treatment room, while the treatment plan is based on a DIBH CT scan. This can possibly induce a systematic setup error corresponding to the movement of the CT markers from FB to DIBH. The standard solution from C-RAD is to calculate the offset by acquiring an additional low dose FB CT, together with the standard DIBH CT. At HGH we developed a solution that does not require an additional FB CT. This method, described below, was used in the CRAM protocol.

In the CT room the patient is setup in FB and aligned with the in-room lasers using two lateral and two longitudinal CT markers. By applying the "CT null" (pressing a button on the scanner controls) this position is now defined as the center of the transversal two-dimensional (2D) CT image matrix. In this position a FB surface scan is acquired with the OS-system. When the patient subsequently performs a breath-hold during the CT acquisition, the CT markers will normally move away from the center position, primarily in the cranial and anterior direction (Figure 3.3A).

In the treatment planning system (TPS, Eclipse v. 13.6, Varian Medical Systems, CA,

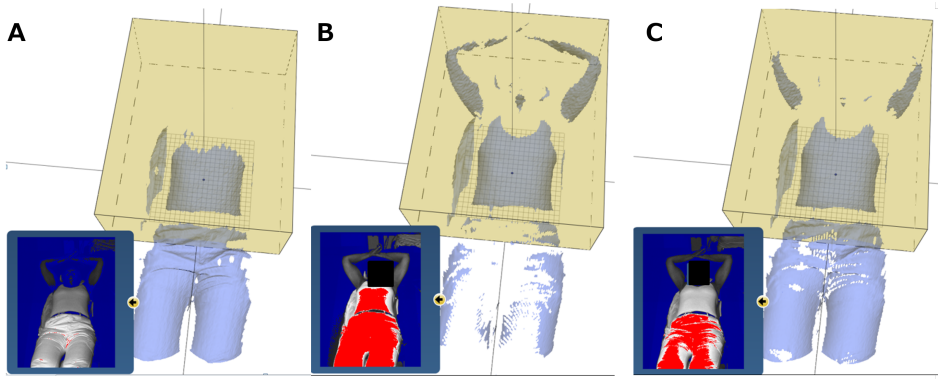

Figure 3.2: Illustration of different camera settings. Gain is set to 400 % for all examples. A: Underexposure with integration time of 2000 μs; arms are not visible in the captured surface. B: Overexposure with integration time of 4500 μs; the red color indicates areas of overexposure, this should be avoided in regions of interest, e.g. at area where the gating gating area is placed. C: Optimal settings with integration time of 3114 μs: as the test person is wearing a t-shirt it is not possible to get more arm surface without overexposure of the belly.

USA) a user-origin is set in the center of the 2D matrix, which corresponds to the original position of the CT markers in FB (Figure 3.3B and C). By doing this, the patient is setup in the CT-markers in FB, and both the tattoo marks and a FB surface reference can be used to setup the patient in the treatment room. A limitation of this is the possibility that the patient moves from time of "CT null", where the surface reference is acquired, to the time of CT scan, which would induce a systematic error throughout the treatment course. In the CRAM protocol the scans were on average 9 ± 3 minutes apart and included placement of the gating area and DIBH training.

3.2.4 Specifics on DIBH and Patient Monitoring

After the initial laser and surface based setup, kv CBCT scans were acquired weekly as part of the CRAM protocol. Before acquisition of the CBCT scans, the couch had to be moved away from the planned treatment position in the lateral and vertical direction, in order to minimize the risk of collision with the gantry of the LINAC. The OS-system cannot handle this movement automatically, and hence the gating area needed to be spatially moved by the radiation therapy technologist (RTT) correspondingly in the lateral direction. This was done by correcting the value identifying the lateral placement of the gating area, in reference to the coordinate system of the LINAC. After CBCT acquisition the couch was moved back to the treatment position and the original placement of the gating area was set.

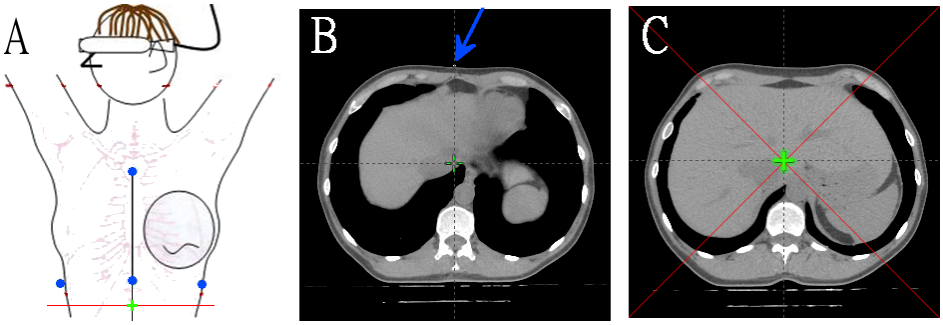

Figure 3.3: Illustration of user-origin placement in TPS. A: The CT markers on the patients (blue dots) breath-hold, and the correct longitudinal placement of the user origin, i.e. the CT markers position at FB (green plus sign). B: One of the CT markers is slightly visible (blue arrow). C: User-origin is set on an imaging slice more caudally than the image from B. The center of the imaging matrix is where the red lines intersect and the user origin should be placed.

Patient monitoring of the whole surface was done in the CRAM protocol. However, a high tolerance for both the length of the error vector and posture errors was set, enabling data collection but avoiding any automatic beam interruptions. Because of the required spatial movement of the gating area prior to CBCT, it was unfortunately not possible to save the respiratory motion signal or the patient monitoring data during CBCT acquisition. The data was saved during the remaining part of the treatment (during e.g. beam delivery and planar imaging). The patient monitoring data was however not analysed due to the deadline of the thesis.

Table 3.1: Characteristics for the patients included in the CRAM protocol

Patient number	Age [years]	Boost [Gy/Fx]	Gating window [mm]	DIBH magnitude [mm]	Time from surface to CT scan [min]	Time from CBCT to kV-MV (max) [min]	Breath-holds per CBCT (max)
1	51		2.5	16.6	8.6	22.2	2
2	61		2.5	16.6	8.0	4.6	2
3	47	10/5	2.0	15.0	7.2	4.7	2
4	70		3.6	17.6	7.1	4.9	4
5	66		2.0	10.7	13.9	9.7	4
6	60		2.0	19.9	9.3	12.3	1
7	64		2.0	9.7	13.0	6.6	2
8	52		3.0	16.8	6.8	5.6	2
9	58		2.4	8.4	9.9	5.3	2
10	72		2.5	21.8	9.9	9.3	2
11	45	10/5	2.0	9.4	5.6	4.4	2
12	54		2.5	17.1	12.0	14.4	1
13	65		2.5	9.3	8.7	4.5	1
14	56		4.0	12.3	7.3	7.7	1
15	62		2.6	18.7	6.5	4.2	2
16	72		3.0	14.9	7.7	4.8	2
17	73		2.5	13.0	6.9	4.8	2
18	54		3.0	13.3	16.7	4.3	3
19	58		2.0	8.6	9.2	4.8	3
20	69		3.0	19.0	9.9	5.3	2
21	67		3.0	12.3	9.1	8.4	3
22	50		3.5	12.9	8.7	3.8	2
23	58		2.5	12.3	4.3	4.3	2
24	60		2.0	7.9	10.8	6.4	3
25	67		2.0	14.2	6.4	16.3	2
26	61		3.5	19.6	8.2	13.1	1
27	35	16/8	3.0	13.7	6.7	3.9	1
28	59		2.5	20.2	9.8	3.4	4
29	49	10/5	3.0	17.8	12.4	5.7	3
30	69		2.5	18.1	5.1	5.3	2
31	55		3.3	16.0	12.5	5.1	4
32	67		2.0	14.0	8.3	5.2	2
33	65		3.0	20.0	9.0	4.2	2
34	69		2.5	14.0	10.6	9.4	2
35	51		2.0	9.0	6.8	4.8	2
36	78		4.0	11.8	16.0	5.5	1
37	79		3.6	9.2	8.5	4.8	6
38							
39	50		3.0	12.9	5.0	8.5	2
40	81		2.0	16.5	6.9	4.7	3
μ	**61**		**2.7**	**14.6**	**9.0**	**6.7**	**2.2**

μ: mean. All patients had the gating area near the xiphoid process, except for patient 13 who had the gating area at the right breast due poor signal reception. Patients received 40 Gy in 15 fractions, except for patient 2 who received 50 Gy in 25 fractions (all with 5 fractions per week). A bold patient number indicates that the patient was included in the pilot study. Patient 38 left the study before fraction 1 (no reason given).

Table 3.2: The OS-installations at HGH developed by C-RAD Positioning AB.

	Installed in	**Installations**	**Room**
Catalyst	End of 2012	8	Treatment
Catalyst	End of 2012	1	Training
Catalyst HD*	End of 2016	1	Treatment
Sentinel	End of 2012	2	CT
Sentinel	End of 2015	1	PET/CT

*The Catalyst HD replaced one of the eight Catalysts in 2016.

CHAPTER 4

Overview of Results and Discussion

In this chapter the main results of the PhD study will be summarized and discussed in a broader context, while the detailed descriptions and reflections can be found in Paper I-III and Appendix A. The discussion will be based on the specific items addressed i.e., the use of an OS-system in regard to patient setup and respiratory motion monitoring; and the dosimetric and positional effects of arm posture correction.

4.1 Pre Irradiation Patient Setup Verification (Paper I)

With Paper I, it was evaluated whether arm posture correction using the OS-system could improve the current setup technique using planar kV-MV images. The prospective study showed no indications of improved kV-MV based setup for patients with arm posture correction. Similar to observations done by Shah et al. [12] and Bert et al. [71], we did identify that arm posture variation occurred despite the use of a breast board. In the present study, arm posture corrections were performed in 85 % of the treatment fractions because the surface differences were above the 5 mm surface tolerance set in the OS-system (Figure 4.1). In addition it was concluded that verification of target position could not be solely based on surface based setup, and that target position verification based on internal anatomy with for example kV-MV is essential. Surface based setup occasionally lead to gross setup errors (>10 mm), and the amount of these were significantly larger than from kV-MV based setup in the longitudinal direction.

It was found that the initial patient position could be significantly improved if based on surface scans rather than laser, also illustrated with a length of the error vector $\leq$ 7 mm in 65 % and 53 % of the treatment fractions for surface (full surface region of interest, ROI_{full}) and laser based setup, respectively (Figure 4.2). The improved patient setup with surface based setup is in agreement with the study by Kügele et al., where the surface (n = 37 patients) and laser (n = 28 patients) based setup were evaluated for breast cancer patients treated in FB, with setup verification using planar field images (MV) [70]. They observed a mean error vector length of 2.5 ± 1.8 and 4.5 ± 4.3 mm (1 SD) for surface and laser based setup, respectively. These mean lengths are smaller than the corresponding vectors from Paper I with median of 5.8 mm (95 % confidence interval (CI): 5.2–6.4 mm)

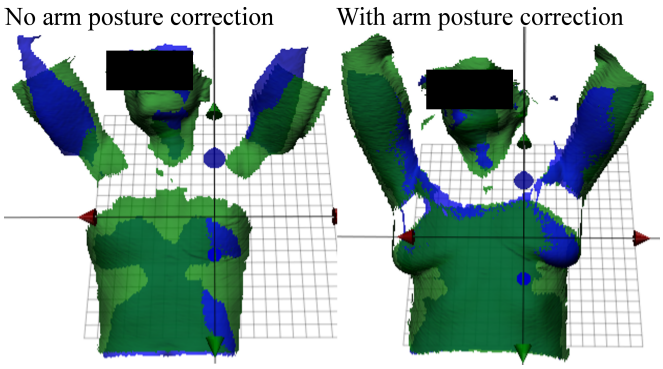

Figure 4.1: Surface scans for two patients. Live surface (blue) and reference surface (green) from the treatment room and CT room, respectively. A patient without (Patient 31) and with (Patient 12) arm posture correction using the OS-system. Data from CRAM protocol.

and 6.5 mm (5.8–7.2 mm). The main differences between the two studies are breathing method (DIBH versus FB) and the ground truth used for evaluation (CBCT versus planar MV). In addition, Kügele et al. excluded the fractions, in which the surface and field images were acquired with more than 5 minutes in between, due to the increased risk that the surface and field images no longer were comparable. An increased time between the scans could contribute to the larger length of the error vector in Paper I; even though the surface and CBCT scan followed directly, the two scans are expected to be minutes apart due to the manual movement of the gating area needed prior to CBCT (explained in subsection 3.2.4). The larger error vector in Paper I can also be explained by the fact that the initial laser and surface based setup were performed in FB, while the kV-MV and CBCT images were acquired in breath-hold; this could lead to larger setup errors especially in the longitudinal and vertical direction. The length of the error vector could also be underestimated in the study by Kügele et al., as a previous study have shown that field images can underestimate the setup error by 20–50 % compared to evaluation based on CBCT [72]. Underestimation of the setup error has also been reported by Bartlett et al. [45] (Table 1.1, page 7).

In Paper I it was found that the surface based setup was improved when ROI_{full} was used for the allignment instead of the more restricted ROIs consisting of the target breast or both breasts. The choice of surface ROI in previous studies is seen to depend on the OS-system in use; with VisionRT the majority have used the target breast [12, 44, 65, 71, 73]; with C-RAD the choice of ROI is often not reported [11, 13–15, 54, 68] or a ROI similar to ROI_{full} [34, 67, 69] have been used. It is suspected that this difference is due to the rigid registration algorithm used by VisionRT and the non-rigid registration algorithm by C-RAD. The latter calculates the posture errors and couch corrections separately, and in

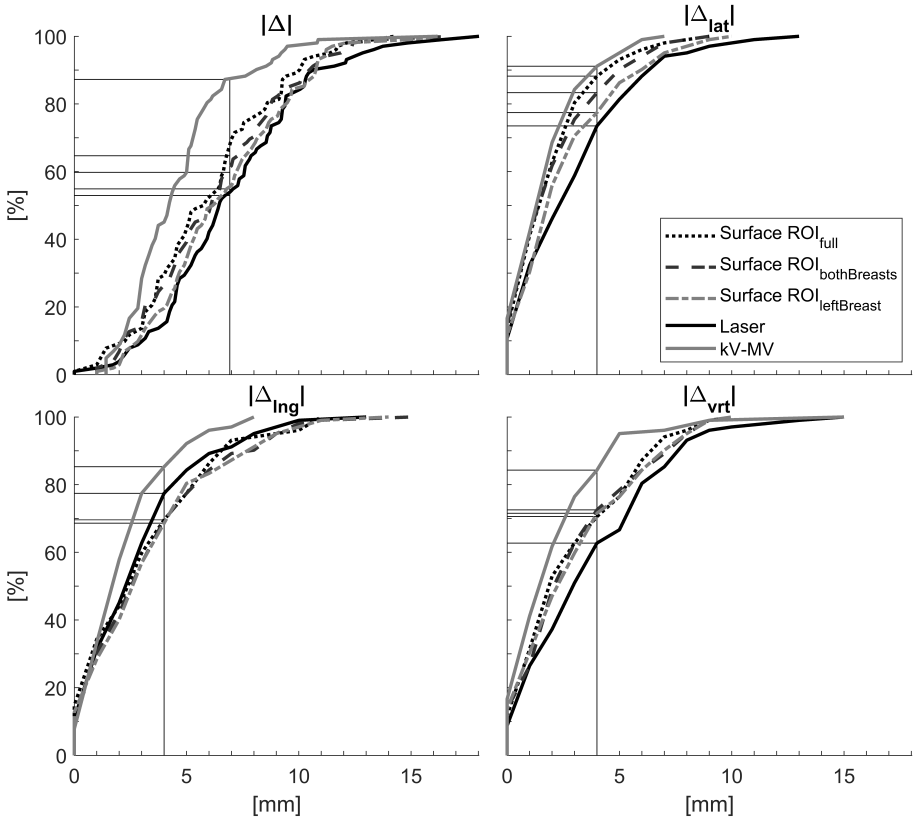

Figure 4.2: Cumulative plots using the different setup techniques with CBCT as ground truth (n = 102 registrations). For the length of the error vector |Δ|, the percentages of setup errors with a radius $\leq \sqrt{48}$ mm are marked with a horizontal line. The percentages of setup errors with a length $\leq$ 4 mm are marked with a horizontal line for the lateral ($|\Delta_{\text{lat}}|$), longitudinal ($|\Delta_{\text{lng}}|$) and vertical ($|\Delta_{\text{vrt}}|$) direction. A single gross setup error based on kV-MV with a length above 10 mm was observed in the vertical direction (15 mm) for patient 29 at fraction 2 (further examined in section 4.3).

addition, the influence of the surface structures are weighted such that surface close to the isocenter has a higher influence. This, together with a potentially more stable registration with ROI_{full} due to more included features [68, 74], might explain the improved setup with ROI_{full} in Paper I.

As rotation errors are not straight forward to correct for with planar imaging, it would be a

benefit if rotation corrections were provided automatically by the OS-system. However, no indication of reduced rotation errors using the surface based setup were found in Paper I. In the study the rotation corrections from the OS-system was evaluated retrospectively and compared to the rotation errors detected by CBCT as the ground truth. As an alternative, the rotation errors detected by the OS-system could have been corrected online by the RTTs in the treatment room, by adjusting e.g. the patient's roll. Subsequently the rotations of the patients could have been evaluated directly using CBCT. This approach might have lead to an alternative conclusion regarding rotation errors, but the present method was chosen to be able to focus on the effect of arm posture correction.

In the current study the single-camera solution was used in combination with calibration using in-room lasers. It is expected that the setup errors from surface based setup would be reduced by using the three-camera solution [75] and by using calibration to the treatment/imaging isocenter. It would be most warranted to investigate if this reduction would be enough to make kV-MV based setup redundant. However, the chest-wall is often used as target surrogate in whole-breast radiotherapy in order to ensure a limited dose to the organs at risk (heart and lungs), and thus it is expected that the conclusion will be unaltered.

4.2 Respiratory Motion Monitoring(Paper II and III)

4.2.1 Phantom Study: Accuracy of Respiratory Motion Monitoring

Paper II evaluated the feasibility of the OS-system for respiratory motion monitoring in radiotherapy using phantoms simulating sinusoidal breathing. The surface motion was measured by tracking an object-marker placed on the surface (RPM) and by tracking the surface directly with an OS-system (Catalyst). It was found that the period estimates from the OS-system and the external marker-based system were similar, while the amplitude estimates from the OS-system were more accurate as they did not depend on the pitch-angle (rotation around the lateral axis) of the tracked surface. In the study, peak-to-peak amplitude errors of approximately 2 mm was observed with a 16° pitch-angle of the object-marker. As pointed out in Paper II, a reproducible patient setup is crucial in radiotherapy, and a reproducible monitoring of the respiratory motion can be achieved with both systems. For the external marker-based system, it does however require that any tilting of the object-marker is reproduced through out the treatment course. We did not investigate to what extent the object-marker tilts in the clinical setting, but claim that it is not possible to completely avoid tilting as the patient's surface is not flat and stable during breathing.

It should be noted that the two-dot marker was investigated in the current study, while newer four- and six-dot markers have been developed showing no roll-dependency (rotation around the longitudinal axis) [76].

4.2.2 Patient study: Interchangeability of Gating Areas

The motive for initiating the study in Paper III was, that we in the clinical use of the OS-system, occasionally found it necessary to spatially move the gating area because of inadequate signal reception in the treatment room. This occurred despite an adequate signal reception in the CT room where the gating area was set (Figure 4.3). In the clinic the problem has only been observed with the one-camera solution (Catalyst) and not with the three-camera solution (Catalyst HD), explained by the better surface coverage (illustrated in Figure 1.5 page 10). But this did occur for one out of the 39 patients in the CRAM protocol, and for four out of the 276 patients included in Paper III. Hence Paper III investigates the feasibility of moving the gating area during the course of treatment, from the area above the xiphoid process or the right breast to the target breast. The area above the xiphoid process was the primary choice for gating area. The right breast was chosen if a xiphoid-near gating area was not possible due to inadequate signal reception in the CT room.

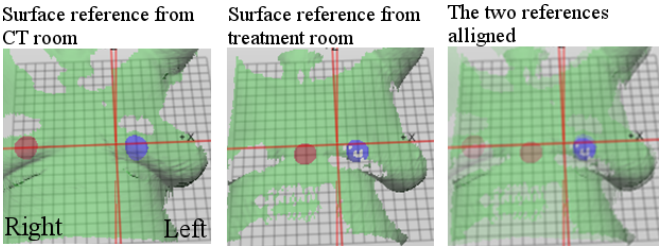

Figure 4.3: Example of spatial movement of the gating area (red circle) from the original placement at the right breast (set in CT room) to the area above the xiphoid process in the treatment room. The inadequate signal reception at the right breast can be verified as holes in the captured surface. In the clinical setting at HGH, the gating area is primarily set at the xiphoid process in the CT room, and if inadequate signal reception occurs it should initially be set at an area that is still near to the xiphoid process; but it can be necessary to set it at the target (if no bolus is present) or contralateral breast.

The feasibility was evaluated using the intra- and inter-fraction reproducibility and stability of the breath-holds measured at the target breast. These breath-holds were measured simultaneously with the breath-holds at the gating area. The stability of the breath-holds was good (SD <2 mm) for all patients; however the study concluded that, in general, the gating area should not be moved as the peak-to-peak difference in breath-hold level measured at the target breast changed more than 5 mm during the treatment course (inter-fraction reproducibility) for the majority of patients (56 %, Figure 4.4). The variation in breath-hold level at the target breast, occurred despite the fact that the breath-hold measured at the xiphoid/right breast was restricted by the gating window. It was found that the peak-to-peak difference in breath-hold during each fraction was within tolerance

($\leq$5 mm) for 82 % of the patients (intra-fraction reproducibility). The maximum observed intra-fraction reproducibility was 18 mm (Figure 4.4).

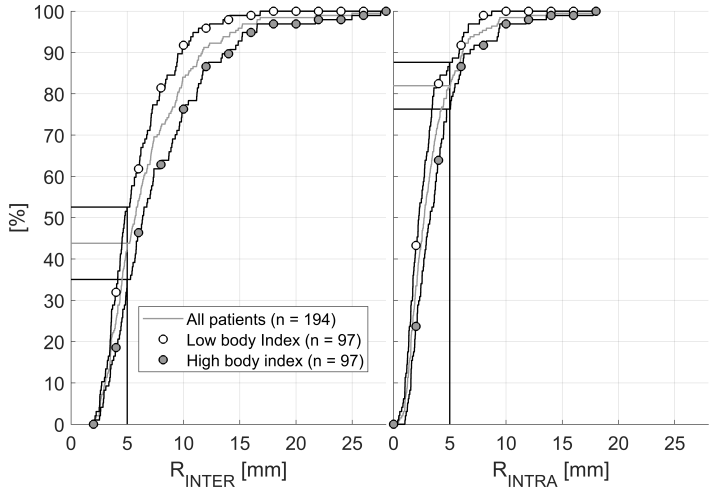

Figure 4.4: Cumulative plot of inter-fraction reproducibility (R_{inter}) and the maximum intra-fraction reproducibility observed for each patient (R_{intra}), of the breath-holds measured at the target breast. Plotted for all patients, patients with low body index ($\leq$ 50th percentile) and patients with high body index (>50th percentile). The percentages of patients that have an acceptable intra- or inter-fraction reproducibility ($\leq$ 5 mm) are marked with a horizontal line.

As stated in Paper III, we did not correlate the respiratory motion signal with the inner anatomy (chest-wall etc.), so basically we do not know which signal best correlates with the position of the target breast. However, good correspondence between the chest-wall and the area above the xiphoid process has been demonstrated in several studies [30, 31, 77]. Some of the variation in breath-hold level, observed at the target breast might be explained by a change in breathing pattern from breath-hold to breath-hold, despite the use of visual guidance. A patient example is discussed in the next section, where a large reduction in lung volume during breath-hold was observed at the treatment compared to the volume at CT scan. As suggested in Paper III, the poor inter-fraction reproducibility could also be a result of the breast being less appropriate as gating area due to its curvature. The gating area is fixed in the room relative to the coordinate system of the LINAC and not to the patient surface, and hence the breast and/or bolus can move in and out of the gating area during breathing motion and from fraction to fraction (due to setup differences), and potentially give rise to differences in the respiratory motion signal.

In Paper III, it was shown that obese patients (with high body index) had larger inter-

fraction variation of the respiratory motion baseline and also had a lower percentage of acceptable intra- and inter-fraction reproducibility. These observations could be explained by our own experience with a more challenging setup for obese patients. Mülliez et al. correpondingly reported an increased SD of the systematic error for patients with BMI> 30 (Σ = 4.9 mm) compared to a BMI <25 (Σ = 1.8 mm)[43]. Their study was based on laser setup for 103 breast cancer patients, evaluated using CBCT as ground truth.

Paper III does not give an answer to what should be done if the signal reception at the gating area is inadequate; but does state that the gating area in general should not be moved to the target breast. However, spatial movement of the gating area from the xiphoid process to a nearby area combined with target position verification both prior and during treatment delivery, should be enough to verify target coverage and OARs sparing. Wiant et al. simulated the worst case scenario with a DIBH plan delivered to a FB patient, who was setup based on CBCT registration using the breast tissue [78]. They found that the dosimetry in regard to heart and target was similar to a plan created and delivered in FB. Based on this a poor inter-fraction reproducibility combined with position verification prior to treatment delivery, would in the worst case be similar to a plan created and delivered in FB. However intra-fraction peak-to-peak difference in breath-hold are difficult to correct for and can hence lead to a shift in the dose distribution with respect to the target. This suggests that the target breast should be avoided as gating area due to the observed peak-to-peak differences in breath-hold of up to 18 mm. In reference to this, it should be noted that a cardinal limitation of the study in Paper III, is that patients were visually guided by the respiratory motion signal measured at the xiphoid process/right breast, and no visual guidance was used for the target breast. Thus, less stability may be expected here.

4.3 Post Irradiation Dose Verification (Pilot Study)

In the pilot study included in Appendix A, the objective was to evaluate the potential dosimetric benefit on dose coverage of the target breast (CTV V_{95}%) using arm posture correction with an OS-system. The dosimetric analysis was illustrated for three CRAM protocol patients (9 CBCT scans). Indications of a reduced CTV dose coverage was found for the fractions with incorrect arm posture (mean $V_{95\%}$ = 97.03 %) compared to the fractions with correct arm posture (mean $V_{95\%}$ = 97.38 %). This could be explained by an increased breast deformation with incorrect arm posture. However, the difference was relatively small and based on a limited number of patients, and could also have arisen due to the uncertainty connected to deformation of the planning CT. The dose coverage of the lumpectomy cavity (CTV_{cavity}, consisting of the visible cavity, clips and a 5 mm margin) was not compromised ($\geq$98 %) for any fractions, reflecting that the treatment plans in regard to the dose coverage of the cavity, is robust towards breast deformations.

Zegers et al. evaluated the treatment plans for 24 breast cancer patients (out of a total of 882 patients) using a new CT scan, due to anatomical inconsistencies observed with

field imaging at treatment [79]. The original treatment plan was recalculated on the new CT and the dose coverage of target breast (CTV V_{95}%) was reduced with 2.6 ± 4.4 % (1 SD) from 99.2 ± 0.6 % (original planning CT) to 96.6 ± 4.4 %. These dose distributions calculated on the new CTs can be compared to the dose distributions caluculated on the deformed planning CTs in the pilot study; they both reflect the patient geometry at treatment delivery. We observed a smaller reduction of 1.8 ± 0.7 % and 1.4 ± 0.7 % with incorrect and similar arm posture, respectively. In the study by Zegers et al. seroma changes was observed in 18 of the 24 patients, which could have a dosimetric effect similar to the effect from breast deformation. In a study by Mourik et al. it was shown that the effect of setup errors, from laser based setup, and breast deformations on the target (breast) coverage, were comparable in magnitude [80]. This reflects that improvement in target coverage could be obtained with reduced breast deformations by e.g. arm posture correction. The CTV coverage reduction in the pilot study give ground to perform the analysis for the remaining patients from the CRAM protocol.

In the current study, the focus was on an incorrect arm posture, but the OS-system can also be used to correct for posture errors in for example the thoracic region and also for rotation errors prior to treatment delivery. If these corrections had been done prior to CBCT acquisition, the estimate of the dose coverage of the target might have been increased, compared to the observed coverage. In addition it should be noted that the alignment of the planning CT and CBCT that was done prior to deformation, did only include translations. It was unfortunately not possible to include rotations in order to be able to perform dose calculations based on the deformed planning CTs in the TPS. Hence any rotation errors will also effect dose coverage of the target when calculated on the deformed planning CT. Based on the CBCT registration from Paper I, a rotation error above 3° (ignoring sign) was observed for two out of the nine included fractions (roll error of 3.9° patient 31, pitch error of 3.1° for patient 25, both for fraction 7).

If the current study design had been paired, the analysis would have been more straight forward and in addition the inter-subject variation would have been eliminated. A paired study design could have been obtained by taking an initial CBCT followed by posture correction, and then an additional CBCT. However, we did not find it feasible for the patient to endure the amount of breath-hold required for two CBCT scans, as each CBCT acquisition took approximately 60 s.

In addition to the investigation on arm posture, one additional patient was examined closer in the pilot study. The patient was suspected to occasionally arch her back to reach the gating window (and not by filling the lungs with air) during breath-hold. This could explain the 15 mm vertical difference that was observed between the setup based on CBCT and the directly following setup based on kV-MV at fraction 2 (Figure 4.2). Deformation of the planning CT to the CBCT at fraction 2 showed a large difference in lung volume, despite the visually guided breath-hold (Figure 4.5). This resulted in an increased dose to the heart at fraction two (V_{17Gy} = 2.50 Gy) compared to the dose derived from the original

treatment plan (V_{17Gy} = 0.62 Gy); the dose was however still below the threshold set by DBCG ($V_{17Gy} \leq$ 5Gy). The dose to the target was not compromised ($\geq$98 %), which can be explained by the initial alignment of the planning CT and CBCT by semi-automatic rigid registration (as in Paper I, but without rotations). Hence, a CBCT based setup is initially performed and subsequently the dose distribution is calculated on the deformed planning CT.

The registration difference of 15 mm in the vertical direction suggests that this specific patient breaths differently from breath-hold to breath-hold despite the use of visual guidance. Hence any setup correction performed at one breath-hold, might not be accurate for the following breath-hold at field delivery. The findings suggest that if the patients is suspected to arch her back during breath-hold, the breath-hold reproducibility should be verified beyond monitoring of the respiratory motion at the gating area; for example by monitoring the whole surface using an OS-system (patient monitoring, section 1.4, page 4), or by field imaging, possibly continuously, during treatment delivery.

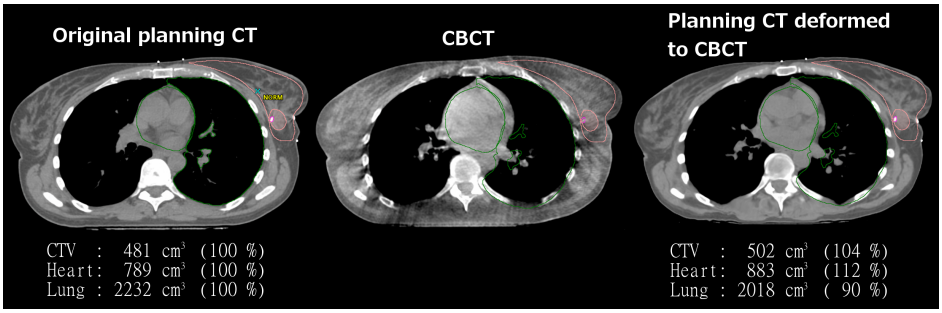

Figure 4.5: Overview of the change in CTV, heart and lung volume from CT room to treatment. The original planning CT, a CBCT acquired at fraction 2, and the planning CT deformed to the CBCT. All depicted structures are the non-deformed structures (CTV, CTV cavity, clips, heart and ipsilateral lung) from the planning CT. The volumes of the CTV, heart and ipsilateral lung are shown together with the percentage difference relative to the volume at planning CT (in parenthesis). The ipsilateral lung is reduced to 90 % of the original volume indicating that the patient might have arched her back to reach the gating window in the treatment room. Shown for patient 29.

CHAPTER 5

Conclusion

The objective of the present PhD was to investigate if the OS-systems can lead to improved radiotherapy for breast cancer patients. The improvement was evaluated in regard to the positioning accuracy of the patient setup, the accuracy of the respiratory motion monitoring, and partly in regard to dose coverage of the target.

It can be concluded that verification of target position with the current technology can not solely be based on OS. Conventional x-ray based imaging of internal anatomy therefore remains an essential part of the clinical workflow. A surface based setup can occasionally lead to gross setup errors (>10 mm). Nevertheless, the initial patient setup is significantly improved if based on surface scans rather than laser. No indications of reduced rotation errors were observed with surface based setup. This might be explained by the applied method where rotation errors detected by the OS-system were corrected retrospectively and not as online corrections by the RTTs in the treatment room.

No indications were found that arm posture correction leads to improved positioning accuracy with the current patient setup technique (kV-MV). On the contrary, a weak non-significant increase in the setup error based on kV-MV was observed. Indications that arm posture correction can improve the dose coverage of the target were seen as a reduction in dose coverage for patients with incorrect arm posture compared to patients with similar arm posture. However, the difference was small and based on a limited number of patients (three patients, 9 CBCT scans).

It has been shown that is feasible to use the OS-system for respiratory motion monitoring. Compared to an alternative external marker-based system, the amplitude estimates from the OS-system is more accurate with no angle-dependency of the patient surface. In the clinical setting it was however discovered that the gating area occasionally (4 out 274 patients) had to be moved from the area above the xiphoid process (primary choice) due to poor signal reception in the treatment room. Hence, the feasibility of moving the gating area to the target breast during the treatment course was investigated in a second study. The study found that the peak-to-peak difference in breath-hold level measured at the target breast changed more than 5 mm during the treatment course for the majority of patients and hence concluded that the gating area in general should not be moved to the target area. The poor signal reception that was encountered with the single-camera solution can most likely be resolved with a three-camera solution in the treatment room.

Overall it can be concluded that the OS-system can improve the radiotherapy for breast

cancer patients, as the system can be used for respiratory motion monitoring with more accurate amplitude estimates. The system can also be used for posture corrections where data indicated that arm posture correction can improve dose coverage of the target. In addition it can be concluded that the OS-system can not replace the conventional patient setup based on x-ray imaging, but the initial patient setup can be improved if based on surface scans rather than laser.

5.1 Future perspectives

Advancement in radiotherapy techniques, such as intensity modulated radiotherapy, volumetric-modulated arc therapy and proton therapy, give the possibility of delivering highly conformal dose distributions with steep dose gradients. Furthermore, margins are sought to be as tight as possible in order to spare the healthy tissue as much as achievable. Radiotherapy for breast usually utilizes simple conformal techniques. However, the tangential fields still offer steep dose gradients towards heart and lung. This requires that the dose distributions are delivered with high accuracy and precision. Compared to less conformal techniques, accuracy and precision is more crucial with tight margins and steep dose gradients, as intra- or inter-fraction errors will have higher consequences.

In the present study intra-fraction errors of up to 18 mm were observed. These large intra-fraction errors can occur when the patient occasionally arches her back to reach the gating window (and not by filling the lungs with air), despite the use of monitoring and visual guidance based on the respiratory motion near the xiphoid process. This illustrates the need for additional patient monitoring during treatment delivery to ensure that gross intra-fraction errors are eliminated. In future studies it would therefore be relevant to investigate whether these errors can be eliminated or reduced by patient monitoring (based on the whole surface) with the OS-system, possibly utilizing the three-camera solution. Arching of the back to reach the gating window, could potentially be detected by monitoring the whole surface and strike out as e.g. a pitch error. A different solution could be to combine the respiratory motion monitoring with the OS-system with an active breathing control (ABC) system using a spirometer, to verify whether the breath-hold level is reached solely by filling the lungs with air. A study on where to position the gating area in order to obtain the strongest correlation between the respiratory motion signal and the inner anatomy (chest-wall) would also be most warranted.

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Appendices

APPENDIX A

Dosimetric Effect of Arm Posture Variation (Pilot Study)

The present is a pilot study on the dosimetric effect of arm posture variation. The analysis is to be performed using the 39 patients from the CRAM protocol (described in Paper I), but due to the deadline of the PhD thesis the analysis could not be done on the whole cohort and is therefore here illustrated for four patients.

Dosimetric Effect of Arm Posture Variation

1. Introduction

Radiotherapy can be used to reduce the risk of both local cancer recurrence and breast cancer death [1]. In radiotherapy it is important that patient geometry is reproduced accurately at each treatment. Patient positioning prior to radiotherapy can be assisted by an optical surface scanning (OS) system, not utilizing ionizing radiation [2–6]. The system can detect deviations between a current (live) surface and an earlier recorded reference surface, and provide corrections for patient posture, e.g. arm posture, and couch adjustments in six degrees of freedom to move the patient to the treatment position. In the current study the focus is on the effect of arm posture variation at treatment delivery compared to the posture at CT scan. Previous studies have highlighted that arm posture variation can occur despite the use of a breast-board for patient positioning [7–9], and it is suspected that incorrect arm posture can lead to deformation of the breast tissue. Batumalai et al. have shown that deformation of breast tissue can lead to deviations between planned and delivered dose [10], but the dosimetric effect of breast deformation caused by arm posture variation has to our knowledge not yet been studied.

The purpose of the present study is to evaluate the dosimetric effect of incorrect arm posture ; in addition the dosimetric effect of large intra-fractional setup variation in the vertical direction is examined for one patient.

2. Materials & Methods

2.1 Patients

Four patients without lymph node involvement scheduled for deep inspiration breath-hold (DIBH) radiotherapy after lumpectomy from the clinical CRAM protocol (described in Paper I) were included in the current study (Table 1). In the protocol the patients were alternately assigned to either arm posture correction using an OS-system (group 2) or no arm posture correction (group 1) and CBCT was acquired weekly. In the current study three patients with incorrect arm posture at treatment compared to the time of CT were selected from group 2. Eligible patients needed to have at least one fraction where the arm posture was similar to the planning CT (Figure 1). In addition the patient (Patient 29) from the CRAM protocol with the largest vertical setup difference (15 mm) between an initial CBCT based setup and a directly following kV-MV based setup was inspected as this could be caused by a large difference in lung volume despite the use of a visually guided DIBH technique.

Table 1: Summary of included patients.

Patient number	17	25	31	29
Age [years]	73	67	55	49
Number of CBCT scans	3	3	3	4
Number of breath-holds per CBCT	2, 2 ,2	1,-[+], 2	3, 3, 4	3, 2, 2, 2
Gating window width [mm]	2.5	2.0	3.3	3.0
Gating amplitude[mm]	13.0	14.2	16.0	17.8

[+]Data was not available. Patient 29 had an additional CBCT as it was suspected that she arched her back during breath-hold. All patients received 40 Gy in 15 fractions, 5 fractions per week.

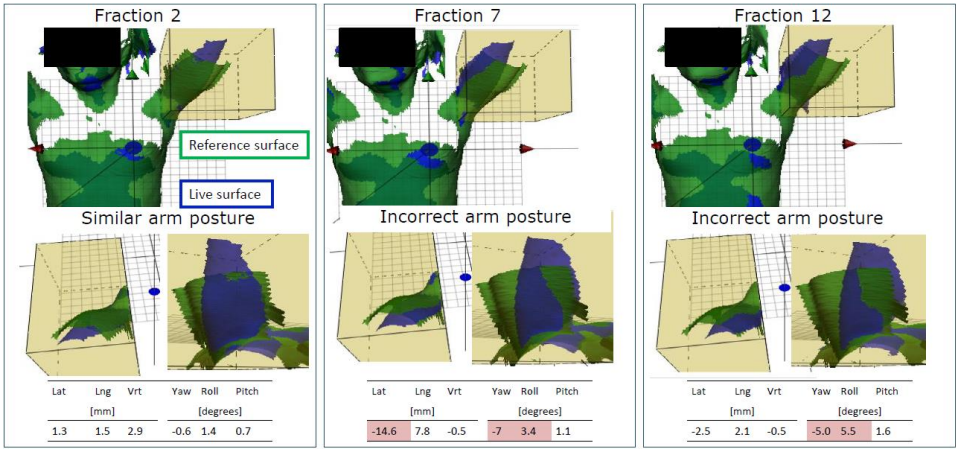

Figure 1: The arm posture variation for patient 31. The surfaces from treatment (blue) have been registered to the reference surface (green) acquired at CT. The numbers in the bottom is the shift that brings the surface of the arm at treatment to the surface of the arm at CT. Incorrect arm posture was identified using these numbers and by visual inspection of the surfaces. Visual inspection was needed as the registration was limited to a small surface area with few features and hence the registration results were not stable. Shifts > 5 mm (in either lat, lng, vrt) or > 3 degrees (in either yaw, roll, pitch) are high-lighted in red.

2.2 Imaging

CT scans were acquired using a 16 slice Philips Brilliance CT Big Bore scanner v. 3.5.17001 (Philips Medical Systems, OH, USA). CBCT were acquired in the treatment room using Varian Clinac iX 2300 linear accelerators equipped with an On-Board Imager (OBI) with the Varian low-dose thorax CBCT protocol. The resolution of the reconstructed CBCT and CT was 1 mm x 1 mm x 2 mm and the CBCT was limited to a scan volume of 45 cm x 45 cm x 16 cm in the lateral, vertical and longitudinal direction, respectively. All scans were performed in DIBH

and respiratory motion was monitored using an OS-system from C-RAD (Sentinel at the CT room and Catalyst in treatment room, C-RAD Positioning AB, Uppsala, Sweden) (Figure 2).

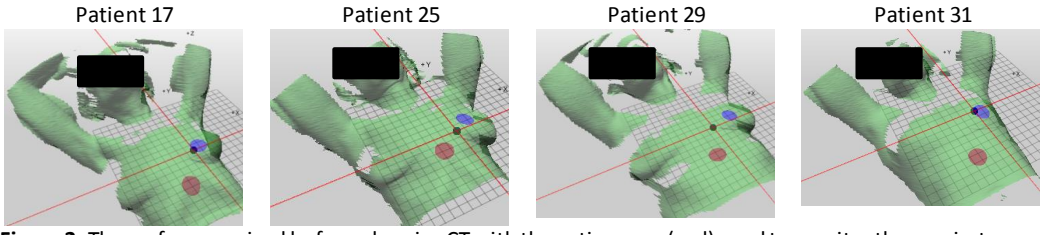

Figure 2: The surface acquired before planning CT with the gating area (red) used to monitor the respiratory motion in the vertical direction. The blue area was also monitored passively but not used in the current study. Preferably, the area above the xiphoid process was used as gating area (Patient 17 and 25). If the signal reception was inadequate, the gating area was moved slightly laterally and caudally (patient 29 and 31).

2.3 Definition of target and organs at risk

Anatomical structures were delineated on the planning CT by radiation oncologists according to national guidelines [11]. Delineation was performed in Eclipse v. 13.6 (Varian Medical Systems, CA, USA) and the structures included the clinical target volume (CTV, whole breast), the lumpectomy cavity (CTV_{cavity}), the heart and ipsilateral lung. Delineation of the lumpectomy cavity was assisted by 4-8 clips inserted during lumpectomy.

2.4 Deformable image registration

The planning CT was initially aligned by semi-automatic rigid registration (translation only, but otherwise as described in Paper I), and subsequently deformed to each CBCT from treatment delivery by deformable image registration (DIR) using SmartAdapt v. 13.6 (Varian Medical Systems, CA, USA) (Figure 3). A description of the applied DIR can be found in the study by Ottosson et al. [12]. The quality of the deformation was visually inspected and did not lead to exclusion of any data. The deformed structures were found by applying the image transformation to the structures from the planning CT. The scan volume was restricted to 16 cm in the longitudinal direction, which means that part of CTV, heart and ipsilateral lung could not always be included in the scan volume (supplementary data, Figure 7). If the structures exceeded the CBCT volume, the original CT scan and structures were used in the analysis (for calculations of structure volumes and dose).

2.5 Dose calculations

All dose calculations were done in the treatment planning system Eclipse v. 13.6. Based on the planning CT, three-dimensional conformal radiotherapy (3D-CRT) treatment plans were originally created using two opposing tangential fields with one or more subfields (field-in-field technique) to obtain a homogeneous dose distribution. Single-energy 6 MV plans were used for three patients, and mixed energies (6 MV or 15 MV) for one patient (patient 25). Treatment plans complied as closely as achievable with the constraints defined by the Danish Breast Cancer Cooperative Group (DBCG). The deformed planning CT was exported from SmartAdapt, and subsequently imported to the treatment planning system. Recalculation of the dose distribution of the deformed planning CT was obtained maintaining treatment fields and monitor units of the original plan (dose

distributions depicted in Supplementary data). By aligning the CBCT and planning CT initially the dose calculations could be performed using patient setup based on CBCT. In this way, focus was set on the breast deformations and not any potential setup errors at treatment.

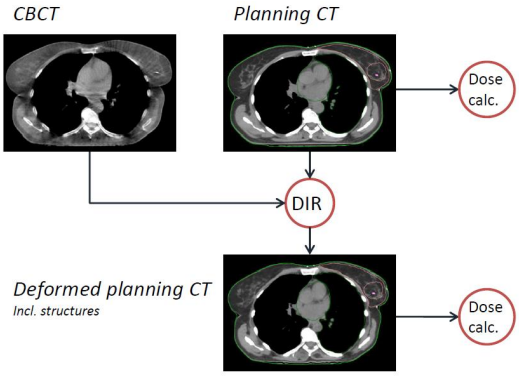

Figure 3: Illustration of the DIR process and dose calculations.

2.6 Data processing

The dose to the organs at risk (OAR) (heart, ipsilateral lung) and the target (CTV and CTV_{cavity}) were compared for the recalculated dose distribution based on the deformed CT and the original dose distribution (calculated based on the planning CT). The target coverage was evaluated by the relative volume of CTV or CTV_{cavity} receiving more than 95 % (38.0 Gy) of the prescribed dose ($V_{95\%}$). $V_{105\%}$ and $V_{108\%}$ for the CTV volume was also extracted, corresponding to the volume receiving more than 42.1 Gy and 43.3 Gy, respectively. The mean dose to the lung was reported, together with the relative volume of the left lung receiving more than 17 Gy (V_{17Gy}). For the heart the calculated values were V_{17Gy} and V_{35Gy}. Plots of the different results were generated in Matlab R2017b (The MathWorks, Inc., Natwick USA).

3. Results

The dose-volume parameters are reported in Table 2. There are indications of a larger reduction in CTV coverage (mean $V_{95\%}$) and a larger variation in $V_{105\%}$ with incorrect arm posture compared to similar arm posture (Table 3 and Figure 4). The dose volume histograms (DVHs) calculated based on the planning CT and deformed CT for patient 31 can be seen in Figure 5.

For patient 29 a reduction in lung volume at fraction 2 is seen in combination with an increase in the heart volume (Figure 6) and hence also an increased dose the heart (Table 2).

Table 2: Results of the treatment planning analysis

Patient number	Treatment plan	Arm posture	CTV_{cavity} [%]	Heart [%]		Ipsilateral lung [%]	[Gy]	CTV [%]		
			$V_{95\%}$	V_{17Gy}	V_{35Gy}	V_{17Gy}	μ	$V_{95\%}$	$V_{105\%}$	$V_{108\%}$
17	TP_{orig}		100.00	1.12	0.15	8.67	4.11	99.36	1.23	0.00
	$TP_{def,2}$	Incorrect	100.00	1.66	0.31	8.35	4.02	**96.98**	1.91	0.00
	$TP_{def,7}$	Incorrect	99.97	1.11	0.07	8.01	3.89	98.55	1.27	0.00
	$TP_{def,12}$	Similar	100.00	1.12	0.14	8.36	4.06	98.42	0.64	0.00
25	TP_{orig}		100.00	3.44	**1.08**	12.84	5.97	**97.46**	0.05	0.00
	$TP_{def,2}$	Incorrect	100.00	2.04	0.39	14.02	6.45	**96.01**	1.36	0.00
	$TP_{def,7}$	Similar	100.00	2.61	0.69	13.11	6.11	**96.45**	0.72	0.00
	$TP_{def,12}$	Incorrect	100.00	0.96	0.04	12.21	5.81	**95.77**	0.42	0.00
31	TP_{orig}		100.00	0.26	0.00	13.26	5.97	99.52	0.04	0.00
	$TP_{def,2}$	Similar	99.77	0.91	0.06	13.04	5.92	**97.26**	0.46	0.00
	$TP_{def,7}$	Incorrect	99.71	0.08	0.00	13.15	5.97	**96.86**	0.33	0.00
	$TP_{def,12}$	Incorrect	99.88	0.30	0.00	13.27	6.03	98.00	0.05	0.00
29	TP_{orig}		100.00	0.62	0.02	12.39	5.70	99.39	1.09	0.00
	$TP_{def,2}$	Similar	100.00	2.50	0.74	12.77	5.80	98.24	0.25	0.00
	$TP_{def,4}$	Similar	100.00	0.00	0.00	12.52	5.77	98.44	0.73	0.00
	$TP_{def,7}$	Similar	100.00	0.00	0.00	11.08	5.27	98.09	**4.47**	**0.01**
	$TP_{def,12}$	Similar	100.00	0.44	0.00	11.74	5.47	98.10	0.71	0.00
DBCG constraint			≥ 98	≤ 5*	≤ 1*	≤ 25	≤ 16	≥ 98	≤ 2	= 0

TP_{orig}: Original treatment plan calculated using the planning CT. $TP_{def,2}$: Treatment plan calculated using the planning CT deformed to the CBCT acquired at fraction 2. μ: mean dose. Bold style indicates that DBCG constraint has been violated. *Extraordinary $V_{17Gy} \leq 10$ % and $V_{35Gy} \leq 5$ % are allowed. The numbers on CTV and OAR coverage are listed in order of the priority set by DBCG (lumpectomy cavity is top priority, followed by OARs, and CTV).

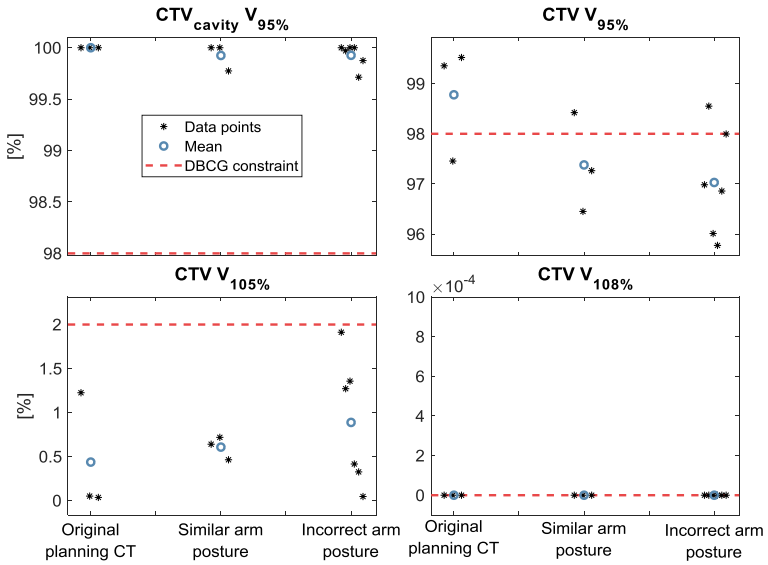

Figure 4: Results for the three patients from the original plan and the deformed plan with incorrect (n =6), similar (n =3) arm posture. Patient 29 not included as any changes are thought to be caused by a difference in breath-hold and not arm posture variation. It should be noted that the labels on the y-axis differ on the different plots for easier view of the differences

Table 3: Target coverage (CTV $V_{95\%}$) for the different calculated dose distributions, for three patients with fractions of incorrect (n =6) and similar (n =3) arm posture. Patient 29 not included.

Patient number	Fraction	TP_{def} [%]	Difference [%] TP_{orig} - TP_{def}	Percentage difference [%] ((TP_{orig} - TP_{def})/ TP_{orig})·100%
Similar arm posture				
17	12	98.42	0.93	0.9
25	7	96.45	1.00	1.0
31	2	97.26	2.26	2.3
mean (1 SD)		**97.38 (1.00)**	**1.40 (0.74)**	**1.4 (0.7)**
Incorrect arm posture				
17	2	96.98	2.37	2.4
17	7	98.55	0.80	0.8
25	2	96.01	1.45	1.5
25	12	95.77	1.68	1.7
31	7	96.86	2.66	2.7
31	12	98.00	1.53	1.5
mean (1 SD)		**97.03 (1.09)**	**1.75 (0.67)**	**1.8 (0.7)**

TP_{orig}: Original treatment plan. TP_{def}: Dose distribution calculated on the deformed planning CT. The numbers used for the calculations are from Table 2. E.g. for patient 17 fraction 12 the difference would be: 99.36 - 98.42 Gy = 0.93 Gy.

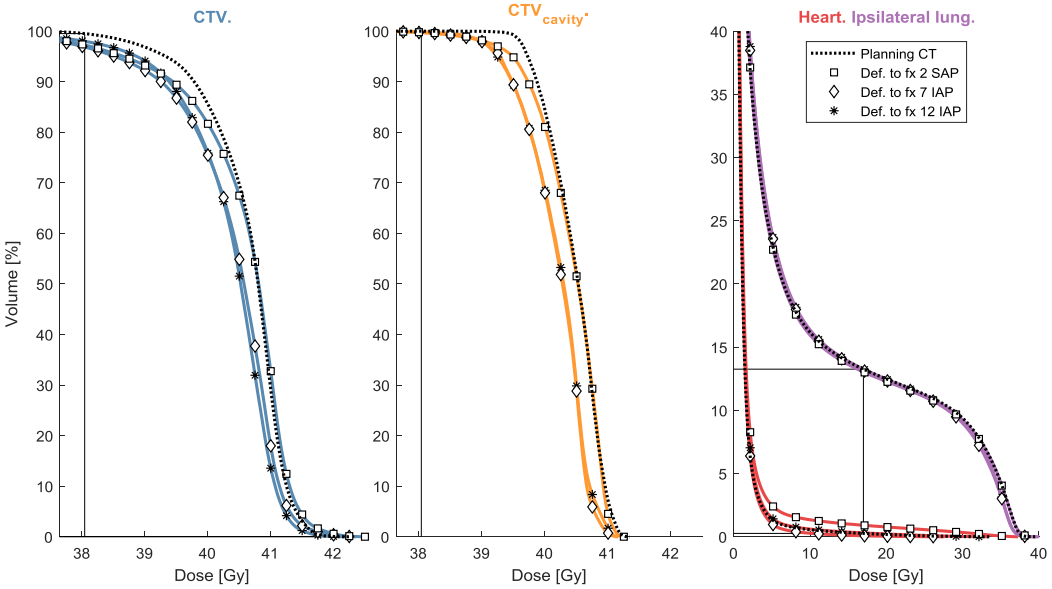

Figure 5: Dose-volume histograms (DVHs) for the different structures based on the original dose plan and the dose distribution based on the deformed (def.) CT. SAP: Similar arm position. IAP: Incorrect arm posture. For the DVH based on the original plan, the reading of $V_{95\%}$ for the CTV and CTV_{cavity}, and of V_{17Gy} for the heart (difficult to see) and the left lung is depicted. Shown for patient 31.

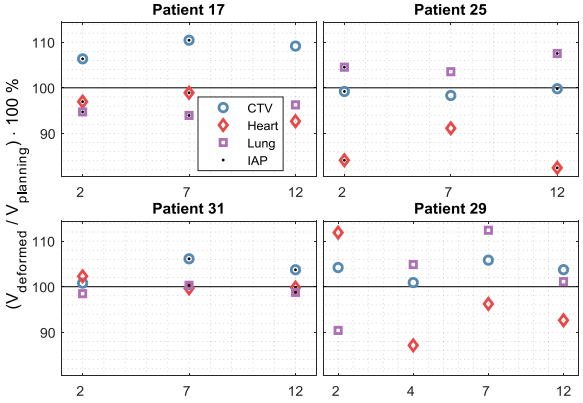

Figure 6: Percentage difference in deformed volume in reference to the volume from planning CT for the four patients. IAP: Incorrect arm posture.

4. Discussion & Conclusion

The main purpose of the present study was to evaluate the dosimetric effect of arm posture variation. Evaluation was done by comparing the dose distributions based on the original planning CT and the planning CT deformed to a CBCT acquired at a treatment fraction just before treatment delivery. Indications of reduced CTV coverage was found for the fractions with incorrect arm posture, while the coverage of the CTV cavity was not compromised for any fractions (≥98%). The findings on CTV coverage is in agreement with arm posture variation giving rise to breast deformation and hence deviation between planned and delivered dose. However, the deviations are relatively small and could also arise due to the uncertainty connected to the deformation of the planning CT. The arm posture variation observed indicates that arm posture correction, for example using an OS-system, can be used to limit breast deformations. Data from three patients is only included in these findings, but give ground to perform the analysis for the remaining 35 patients from the CRAM protocol.

In the current study patients without lymph node involvement are studied, and hence the CTV included the breast but not the axillary and supraclavicular lymph node areas. For patients where the nodes are part of the CTV it is suspected that arm posture variation could lead to greater CTV-tissue deformation and hence also have a greater influence on target coverage. However, with the limited field of view for the CBCT the main part of these lymph node regions are not included, and thus in order to study this further would require that a single CBCT in this area was acquired or two consecutive CBCTs were acquired.

The findings for patient 29 show that relatively large intra-fractional lung volume variation can be observed which can lead to an increased dose to the heart. The variation can be explained by the patient occasionally arching her back to reach the gating window (and not by filling the lungs with air) or be caused by the gating area placement at the belly which allows the patient to use predominately abdominal breathing to reach the gating window at some fractions, while others using a combination of both abdominal and thoracic breathing.

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6. Supplementary data

The field of view of the CBCT is illustrated in Figure 7. The dose distribution calculated on the planning CT and the deformed CT (planning CT deformed to the CBCT) are visualised for one slice in Figure 8, Figure 9, Figure 10 and Figure 11.

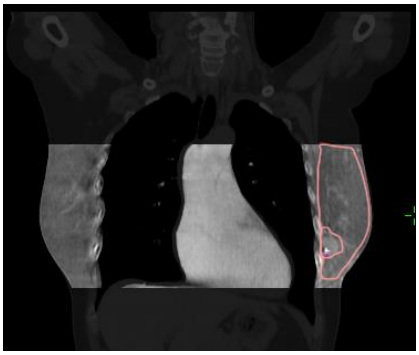

Figure 7: Field of view of the CBCT limited to 16 cm in the longitudinal direction. The CBCT is visualized in light grey tones, while the planning CT can be visualized in darker grey.

17 Dose distribution calculated using planning CT or planning CT deformed to CBCT at the different fractions.

With non-deformed contours from planning CT (clips, visible lumpectomy cavity, CTV, heart, ipsilateral lung, body).

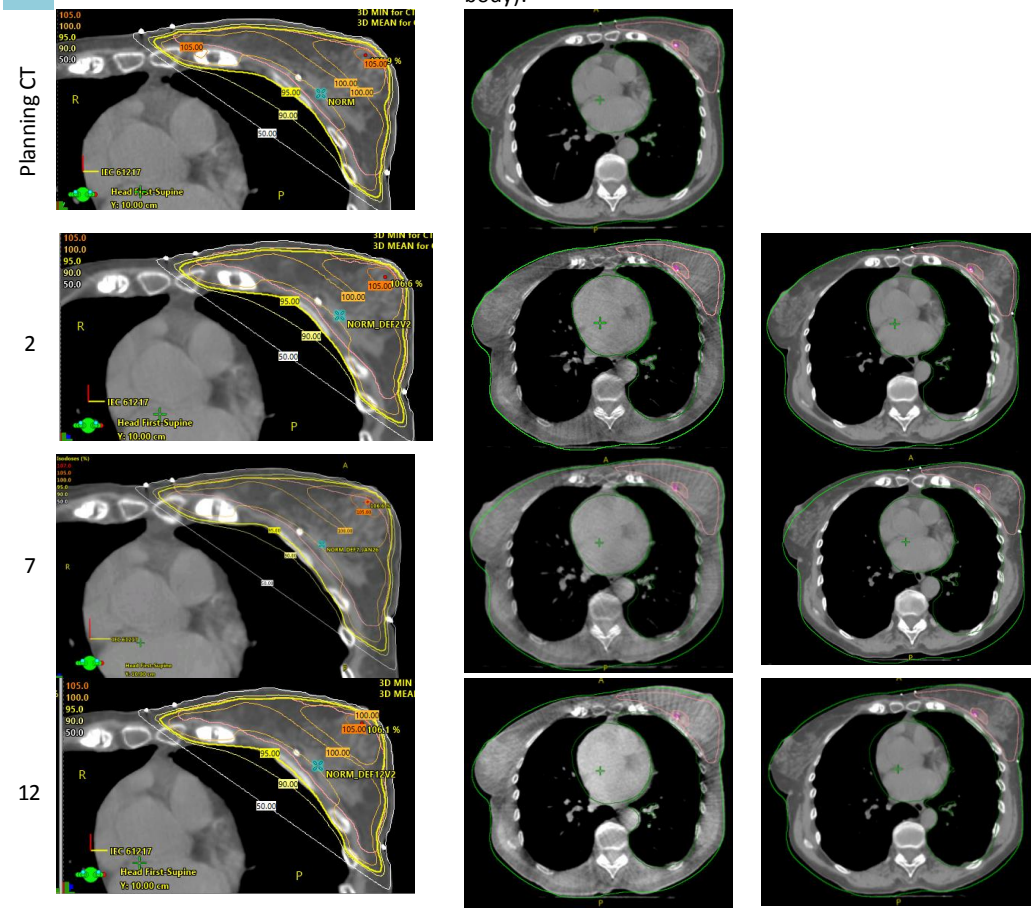

Figure 8: The dose distributions calculated on the original planning CT and the planning CT deformed to the CBCT acquired at fraction 2,7, and 12. Patient 17.

25 Dose distribution calculated using planning CT or planning CT deformed to CBCT at the different fractions.

Planning CT or CBCT | Deformed planning CT

With non-deformed contours from planning CT (CTV, heart, ipsilateral lung, body).

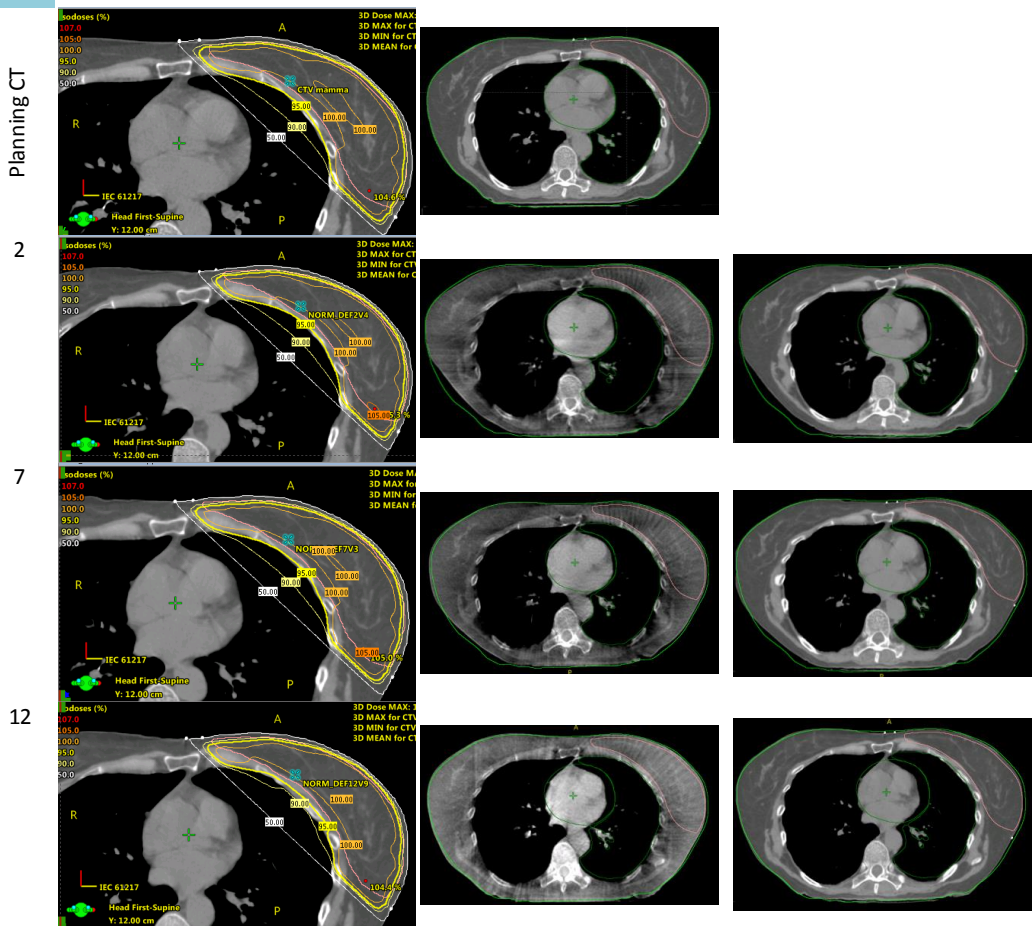

Figure 9: The dose distributions calculated on the original planning CT and the planning CT deformed to the CBCT acquired at fraction 2, 7, and 12. Patient 25.

Patient 29 Dose distribution calculated using planning CT or planning CT deformed to CBCT at the different fractions.

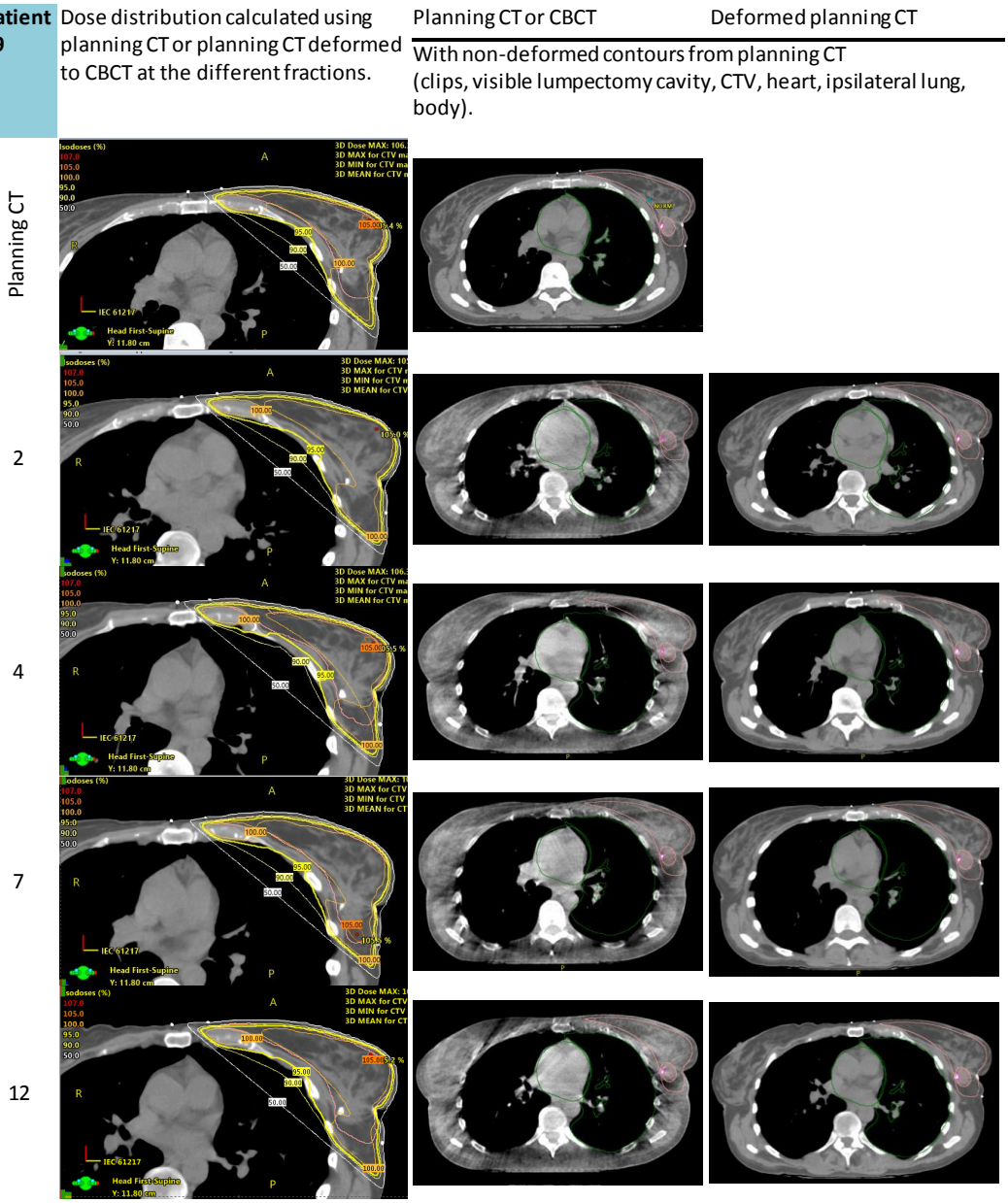

Figure 10: The dose distributions calculated on the original planning CT and the planning CT deformed to the CBCT acquired at fraction 2, 7, and 12. Patient 29.

Patient 31	Dose distribution calculated using planning CT or planning CT deformed to CBCT at the different fractions.	Planning CT or CBCT	Deformed planning CT
		With non-deformed contours from planning CT (visible lumpectomy cavity, CTV, heart, ipsilateral lung, body).	

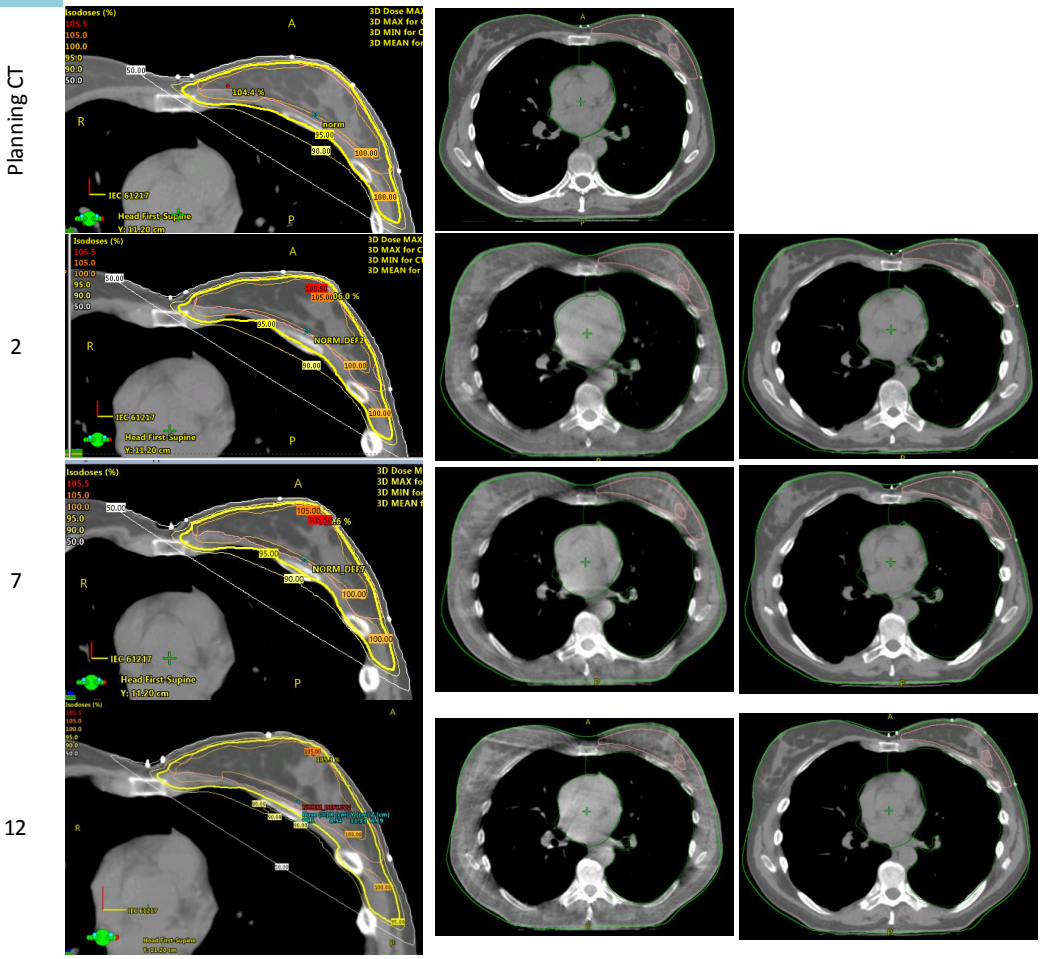

Figure 11: The dose distributions calculated on the original planning CT and the planning CT deformed to the CBCT acquired at fraction 2, 7, and 12. Patient 31.

APPENDIX B

CRAM Protocol (in Danish)

This chapter includes the clinical CRAM protocol, the information for patients, treatment guidelines and a treatment schedule handout. All in Danish.

B.1 Protocol

Forsøgsprotokol Anmeldelsesnummer: 49450

Version 3 5. november 2015

Evaluering af overfladeskannings-system for venstre-sidig brystkræft patienter planlagt til postoperativ DIBH strålebehandling (CRAM)

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Ansvarlig klinisk teknisk specialist: Susanne Lind.
Ansvarlig radiograf: Janne Nørlykke Drudgaard.

Forsøgssted:
Stråleterapien, Onkologisk afdeling, Herlev og Gentofte Hospital (HGH), Herlev Matriklen.

1. Forsøgets formål

Forsøgets formål er at undersøge om et optisk overfladeskannings(OS)-system kan være med til at øge nøjagtigheden af strålebehandlingen så den leverede dosis til risikoorganer(hjertet og lunger) og target(brystet) er bedre i overensstemmelse med det planlagte. På den måde undersøges om OS-systemet kan forbedre strålebehandlingen for venstre-sidige brystkræft patienter.

2. Baggrund

Brystkræft er den hyppigste kræftform hos kvinder og udgjorde 26 % af alle nye kræfttilfælde for kvinder i 2012 [1]. De fleste brystkræftpatienter tilbydes adjuverende strålebehandling for at reducere risikoen for både lokalrecidiv og brystkræftdødsfald. Fem års overlevelse for brystkræftpatienter er på 85 % [2]. Der er påvist en øget hjertedødelige for patienter med venstre-sidig brystkræft efter strålebehandling [3], og risikoen for at udvikle iskæmisk hjertesygdom er proportional med gennemsnits stråledosis til hjertet [4].

Strålebehandlingen gives normalt som 25 fraktioner, en fraktion per dag, 5 dage om ugen. Behandlingen planlægges ud fra en CT skanning af patienten, taget få dage før behandlingen starter. Det er derfor afgørende at patienten ligger i samme position ved hver fraktion, for at sikre at strålingen bliver leveret præcis som planlagt. Ved den nuværende positioneringsteknik placeres patienten i en støtteskal med støtte til armene og

hovedet, for at sikre patienten ligger i samme position. Derudover bruges tatoveringsprikker på patienten som sammen med in-room lasere bruges til at sikre den korrekte position. Som positioneringskontrol tages 2D megavoltage billeder.

Hvis patientens holdning er forkert, fx hvis armen er placeret anderledes [5], vil dette kunne ændre brystvævets placering, hvilket ikke vil blive opfanget ved den nuværende praksis. Daglige 3D røntgenbilleder i form af cone beam CT (CBCT) vil delvist kunne bruges, men de indfører en yderligere dosis til patienten, og armene vil være udenfor skanningsfeltet.

Et alternativ, der ikke giver yderligere stråledosis til patienten, er et laser-baseret overfladeskannings(OS)-system. Systemet kan registrere forskellene imellem en nuværende OS og en tidligere optaget reference OS. Denne registrering kan korriggere patientens holdning, fx armens placering, men kan også give lejejusteringer inden behandlingen startes.

Der er lavet undersøgelser der viser at OS-systemer har god korrelation med CBCT for brystkræft patienter, [6][7]. Desværre ved vi ikke hvor stor dosimetrisk fordel der er ved at anvende OS-systemet til positionering af patienter med brystkræft. Det vil vi klarlægge med dette forsøg. Vi vil undersøge om dosis til risikoorganer og target er i bedre overensstemmelse med det planlagte, og dermed om strålebehandlingen er forbedret, når OS-systemet bruges.

3. Forsøgets metode

To patientgrupper undersøges, en kontrolgruppe der skal følge den nuværende positioneringsteknik, og en indsatsgruppe der yderligere skal positioneres med OS-systemet. Det er kun patienter der har givet tilsagn om at deltage i studiet og underskrevet samtykkeerklæringen der inkluderes.

Inden strålebehandlingen starter bruges den samme positioneringsteknik for begge grupper, men for indsatsgruppen anvendes OS-systemet lige inden de daglige 2D megavoltage billeder. Ud fra systemets korrektioner, vil patientens holdning blive rettet til, fx armens placering, og dernæst vil patients leje eventuelt blive flyttet baseret på OS-systemet analyse. Patientens position bliver som vanligt kontrolleret med standard 2D megavoltage billede.

For at undersøge den dosimetriske effekt af positionering med OS-systemet laves ugentlige 3D røntgenbilleder (CBCT) for begge grupper. Dette er nødvendigt for at få et billede af patientgeometrien ved behandlingen, som så kan bruges til at lave dosisberegninger. Disse dosisberegninger kan fortælle os om strålebehandlingen er forbedret når OS-systemet bruges.

4. Statistiske overvejelser

T-test vil blive brugt til at vurdere den statistiske signifikans af fund. Det vil blive undersøgt om dosis til risikoorganerne (hjertet og lunger) og til target (brystet) er i bedre overensstemmelse med det planlagte når OS-systemet bruges.

Hjertet formodes være den struktur, hvor den mindste dosisforskel skal detekteres, og dermed den struktur som vil kræve det største antal inkluderede patienter.

Det formodes at positionering med OS-systemet kan reducere gennemsnitsdosis til hjertet med 10 % fra 2.5 Gy [8] til 2.25 Gy, og at standardafvigelsen er 0.25 Gy. Med α= 0.05 og en styrke på 80 %, skal der dermed indgå ∼40 patienter i forsøget for at opnå en tilstrækkelig statistisk styrke til at påvise en reduktion i gennemsnitshjertedosis.

5. Patienter

I forsøget inkluderes 40 patienter, heraf tyve patienter i kontrolgruppen.

5.1 Inklusionskriterier

- Patienter med venstre-sidig brystkræft uden lymfeinvolvering henvist til DIBH strålebehandling på Herlev og Gentofte Hospital (HGH), Herlev Matriklen.
- Skal kunne forstå mundtlig og skriftlig information på dansk.
- Underskrevet informeret samtykkeerklæring og udleveret patientinformation.

5.2 Eksklusionskriterier

- Gravide eller ammende.

7. Datatilsyn

Oplysninger om forsøgspersonen beskyttes efter lov om behandling af personoplysninger og sundhedsloven. Projektet er endvidere anmeldt til Datatilsynet d. 21/9 2015.

8. Økonomiske forhold

Der gives ikke honorar til medvirkende patienter. Det er ph.d.-studerende Susanne Nørring Bekke som har taget initiativ til dette projekt. Hendes studier er finansieret af Center for Nukleare Teknologier ved Danmarks Tekniske Universitet (DTU) samt Stråleterapien ved Herlev og Gentofte Hospital (HGH), Herlev Matriklen

Der er ikke nogle firmafinansieret fondsstøtte i forbindelse med projektet. Teknisk udstyr og lokaler stilles til rådighed af Stråleterapien på HGH.

9. Hvervning af deltagere

Patienterne vil blive søgt hvervet til dette projekt når de møder ind i forbindelse med deres planlagte behandlingsforberedende CT skanning, på Onkologisk Afdeling, HGH, Herlev Matriklen. I forbindelse med den mundtlige information udleveres samtidigt den skriftlige patientinformation, og det fortrykte tillæg ”Forsøgspersoners rettigheder i et sundhedsvidenskabeligt forskningsprojekt”. Patienten gives betænkningstid og mulighed for yderligere samtale. *Se også bilaget med retningslinjer for den mundtlige information*.

10. Offentliggørelse af forsøgsresultater

Resultaterne af forsøget, negative, positive samt inkonklusive, vil blive offentliggjort og fremlagt på faglige konferencer i ind-og udland, og eventuelt publiceret i internationale anerkendte tidskrifter inden for området.

11. Videnskabsetisk redegørelse

Der er ikke nogle ekstra risici ved positionering med OS-systemet i forhold til den rutinemæssige opstilling; dog vil den enkelte patient i forsøget få en ekstra stråledosis. Derudover kan patienten dagligt forvente ca. 5 minutter ekstra på lejet ved positionering med OS-systemet, ligesom det ugentligt vil tage ca. 15 minutter ekstra pga. de ekstra billedundersøgelser. Den første ekstra billedundersøgelse vil en fysiker bruge til at lave en ekstra kvalitetskontrol af behandlingen.

Det nuværende forsøg vil redegøre for om OS-systemet giver en forbedret strålebehandling for venstre-sidige brystkræft patienter. Forsøget har stor klinisk relevans da det vil kunne fortælle om OS-systemet skal bruges til positionering fremover.

Det har stor betydning hvis det viser sig at OS-systemet er med til at giver en mindre dosis til hjertet end ellers, da risikoen for at udvikle iskæmisk hjertesygdom er proportional med gennemsnits stråledosis til hjertet. Hvis OS-systemet er med til at forbedre dækningen af target (brystet) vil det være med til at reducere risikoen for lokalrecidiv.

a. Stråledosis

Ved planlægningen af strålebehandlingen vil patienten få foretaget en rutinemæssig CT skanning, hvilket giver patienten en stråledosis på 10 mSv, se Tabel 1. Til sammenligning er den naturlige baggrundsdosis i Danmark 3 mSv/år. Det skal bemærkes at denne CT-skanning er en del af standardbehandlingen, og giver altså ikke nogen ekstra dosis til patienten.

I forbindelse med forsøget vil patienterne få en ekstra stråledosis, fortrinsvist i behandlingsområdet, på grund af de ekstra 3D røntgenbilleder (CBCT).

CBCT'erne giver en effektiv dosis på 5 mSv/billede [9]. Med 3-6 CBCT'er per patient, fås en total ekstra dosis på ca. **15–30 mSv.** Antallet af CBCT'er afhænger af om patienten behandles i 3 uger (40 Gy/ 15 fraktioner) eller 5 uger (50 Gy/ 25 fraktioner) og om boost (10 Gy/5 fraktioner eller 16 Gy/8 fraktioner) er inkluderet i behandlingen. Hvis boost er inkluderet tages én ekstra CBCT.

En total ekstra dosis på 30 mSv svarer til ca. 10 års baggrundsstråling. I den raske befolkning vil denne ekstra stråledosis øge risikoen for at introducere en uhelbredelig cancersygdom med ca. 0,15 procentpoint, fra den generelle risiko på 25 % til 25,15 % [10]. Dermed er der en lille øget risiko for stokastiske skader, som fx en ny uhelbredelig cancersygdom, en såkaldt stråleinduceret sekundær cancer. Sammenholdt med den langt større stråledosis patienterne modtager i terapeutisk øjemed (40-66 Gy, hvor 66 Gy med fotonbestråling svarer til ca. 66.000 mSv [organvægtningsfaktor = 1, strålevægtningsfaktor = 1]), er den ekstra stråledosis i forsøget lille, og holdes under tærskelværdien for deterministiske skader.

Vi konkluderer derfor at risikoen for at dø af sekundær cancer forårsaget af strålebehandlingen er langt højere end risikoen for at dø af en eventuelt strålingsinduceret sekundær cancer på baggrund af de ekstra CBCT.

	Frekvens	Stråledosis [mSv]
Standardbehandling		
CT skanning	1 gang	10 mSv
Ekstra ved forsøg		
3-6 CBCT skanninger	Ugentligt	15-30 mSv*
Positionering med OS	Dagligt	0

Tabel 1: Forsøgsforløb og ekstra dosis ved deltagelse i forsøget. * Afhængig af antallet af fraktioner, vil der i alt blive lavet mellem 3 og 6 CBCT for den enkelte patient, hvor en CBCT svarer til en effektiv dosis på 5 mSv/billede.

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B.2 Information for Patients

Deltagerinformation Anmeldelsesnummer: 49450

Version 6 4. maj 2016

Evaluering af overfladeskannings-system for brystkræft patienter planlagt til strålebehandling

Vi vil spørge, om du vil deltage i et videnskabeligt forsøg.

Det er frivilligt at deltage i forsøget. Du kan når som helst og uden at give en grund trække dit samtykke tilbage. Det vil ikke få konsekvenser for din videre behandling.

Forsøget udføres ved Stråleterapien på Herlev Hospital.

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Original titel: Evaluering af overfladeskannings-system for venstre-sidig brystkræft patienter planlagt til postoperativ DIBH strålebehandling (CRAM).

Forsøget har til formål at undersøge om et overfladeskannings-system kan bruges til at give en forbedret strålebehandling for venstre-sidige brystkræft patienter.

Forsøget indebærer:

- fem minutter ekstra dagligt på lejet før behandling hvis vi skal positionere dig med overfladeskannings-systemet.
- Femten minutter ekstra én gang om ugen til at tage ekstra 3D røntgenbilleder.
- En ekstra kvalitetskontrol af din strålebehandling.
- På grund af de ekstra 3D røntgenbilleder, vil du blive udsat for en ekstra stråledosis, svarende til ca. 10 gange den årlige baggrundsbestråling i Danmark.

I den vedlagte deltagerinformation kan du læse mere om, hvad forsøget går ud på, hvad der vil ske med dig, og dine rettigheder, hvis du siger ja.

Deltagerinformation Anmeldelsesnummer: 49450

Version 6 4. maj 2016

Deltagerinformation om deltagelse i et videnskabeligt forsøg.

Evaluering af overfladeskannings-system for brystkræft patienter planlagt til strålebehandling

Vi vil spørge, om du vil deltage i et videnskabeligt forsøg, der udføres af ph.d.-studerende Susanne Nørring Bekke.

Før du beslutter, om du vil deltage i forsøget, skal du fuldt ud forstå, hvad forsøget går ud på, og hvorfor vi gennemfører forsøget. Vi vil derfor bede dig om at læse denne deltagerinformation grundigt.

Du vil blive inviteret til en samtale om forsøget, hvor denne deltagerinformation vil blive uddybet, og hvor du kan stille de spørgsmål, du har om forsøget. Du er velkommen til at tage et familiemedlem, en ven eller en bekendt med til samtalen.

Hvis du beslutter dig for at deltage i forsøget, vil vi bede dig om at underskrive en samtykkeerklæring. Husk, at du har ret til betænkningstid, før du beslutter, om du vil underskrive samtykkeerklæringen.

Det er frivilligt at deltage i forsøget. Du kan når som helst og uden at give en grund trække dit samtykke tilbage. Det vil ikke få konsekvenser for din videre behandling.

Baggrund
Strålebehandling gives over flere små doser (fraktioner), hvor der gives en fraktion per dag - 5 dage om ugen. Selve strålebehandlingen planlægges ud fra en CT skanning, taget få dage før behandlingen starter. Ved hver fraktion er det derfor vigtigt at patienten ligger på samme måde for at sikre at strålingen bliver leveret som planlagt.

I den nuværende praksis placerer vi patienten i en støtteskal med støtte til armene og hovedet, for at sikre patienten ligger i samme position. Derudover bruges tatoveringsprikker på patienten, som sammen med lasere bruges til at sikre den korrekte position. Som kontrol tager vi også røntgenbilleder før strålingen leveres.

Denne praksis kan dog ikke fortælle os noget om patientens holdning, fx hvis armen er i en forkert position. Yderligere sikring af patientens position (*positionering*) kan vi få med et overfladeskannings-system, som er baseret på laserlys, og derfor ikke giver yderligere stråledosis. Dette system er brugt på flere stråleterapi afdelinger, men der mangler undersøgelser der viser om systemet gør strålebehandlingen mere præcis.

Formål med forsøget
Formålet med forsøget er at undersøge om overfladeskannings-systemet kan bruges til at give en forbedret strålebehandling for patienter med venstre-sidig brystkræft.

Hvad indebærer forsøget
I forsøget vil der indgå 40 patienter, hvoraf ca. 20 patienter vil positioneres som sædvanligt (kontrolgruppe), mens resten også vil blive positioneret med overfladeskannings-systemet (indsatsgruppe). Uanset gruppe, vil der stadig blive taget de sædvanlige kontrolbilleder for at sikre at strålebehandlingen udføres korrekt. Der er tilfældigt hvilken gruppe du ender i.

Deltagerinformation Anmeldelsesnummer: 49450

Version 6 4. maj 2016

Hvis du er en del af indsatsgruppen vil personalet ved behandlingsapparaterne, bruge overfladeskannings-systemet til evt. at justere på din holdning. Det kan være din arm skal rettes ind eller dit hoved skal drejes, for at du ligger i samme position som du gjorde ved den oprindelige CT skanning. Derudover kan det være at lejet som du ligger på skal rykkes en anelse. Du kan godt forvente at dette dagligt vil tage ca. 5 minutter mere end det ellers ville have gjort.

Som en del af forsøget vil du få lavet mellem 3 og 6 ekstra 3D røntgenbilleder (cone beam CT), som skal bruges til at vurdere om overfladeskannings-systemet er med til at give en forbedret strålebehandling. De ekstra røntgenbilleder vil blive taget ugentligt, og antallet af billeder afhænger af hvor mange behandlingsdage(fraktioner) du har. Det første sæt 3D røntgenbilleder vil en fysiker bruge til at lave ekstra kvalitetskontrol af din strålebehandling.

Forsøget kræver ikke ekstra fremmøder eller forberedelse.

Nytte ved forsøget
Det er vores håb at vi ved dette forsøg kan vise om positionering med et overfladeskannings-system kan bruges til at give en forbedret strålebehandling af brystkræft. Forsøget skal på denne måde afklare om overfladeskannings-systemet skal bruges for brystkræft patienter fremover.

Bivirkninger, risici, komplikationer og ulemper
Der er ikke nogen ekstra risici ved positionering med overfladeskannings-systemet, men du skal regne med at behandlingen dagligt tager 5 minutter ekstra. Derudover skal du regne med at det tager ca. 15 minutter mere end vanligt de ugentlige dage, hvor du får lavet ekstra 3D røntgenbilleder

På grund af de ekstra 3D røntgenbilleder i forbindelse med forsøget, vil du blive udsat for ekstra stråledosis mod brystkassen, svarende til ca. 10 gange den årlige baggrundsbestråling i Danmark (3 mSv/år). Selve strålebehandlingen giver en langt større stråledosis. For raske forsøgspersoner er risikoen for at dø af kræft 25 % i Danmark. Ekstra skanningerne vil øge denne risiko med 0,15 procentpoint fra den generelle risiko på 25 % til 25,15 %.

Der kan være risici ved forsøget, som vi endnu ikke kender. Vi beder dig derfor om at fortælle, hvis du oplever problemer med dit helbred, mens forsøget står på. Hvis vi opdager bivirkninger, som vi ikke allerede har fortalt dig om, vil du naturligvis blive orienteret med det samme, og du vil skulle tage stilling til, om du ønsker at fortsætte i forsøget.

Deltagelse og afbrydelse af forsøg:
Det er frivilligt at deltage i forsøget. Du kan når som helst og uden at give en grund trække dit samtykke tilbage, uden at det vil få konsekvens for din videre behandling.

Oplysninger om økonomiske forhold
Der gives ikke honorar til medvirkende patienter. Det er ph.d.-studerende Susanne Nørring Bekke som har taget initiativ til dette projekt. Hendes studier er finansieret af Center for Nukleare Teknologier ved Danmarks Tekniske Universitet (DTU) samt Stråleterapien ved Herlev Hospital.

Der er ikke nogle firmafinansieret fondsstøtte i forbindelse med projektet. Teknisk udstyr og lokaler stilles til rådighed af Stråleterapien.

Deltagerinformation Anmeldelsesnummer: 49450

Version 6 4. maj 2016

Adgang til forsøgsresultater
Resultaterne fra undersøgelsen, negative såvel som positive, samt inkonklusive resultater vil blive offentliggjort og fremlagt på faglige konferencer i ind- og udland, og publiceret i internationale tidsskrifter indenfor området.

Forsøgskontrol
Samtykket omfatter adgang til videregivelse og behandling af nødvendige oplysninger om dit helbred og evt. andre fortrolige oplysninger som led i relevante myndigheders kontrol med forsøget.

Vi håber, at du med denne information har fået tilstrækkeligt indblik i, hvad det vil sige at deltage i forsøget, og at du føler dig rustet til at tage beslutningen om din eventuelle deltagelse. Vi beder dig også om at læse det vedlagte materiale "Forsøgspersonens rettigheder i et sundhedsvidenskabeligt forsknings-projekt".

Hvis du vil vide mere om forsøget, er du meget velkommen til at kontakte:

Afdelingssygeplejerske Nana Hviid Dinesen, tlf. 3868 2377 (hverdage 8.30-15).

Med venlig hilsen

Susanne Nørring Bekke

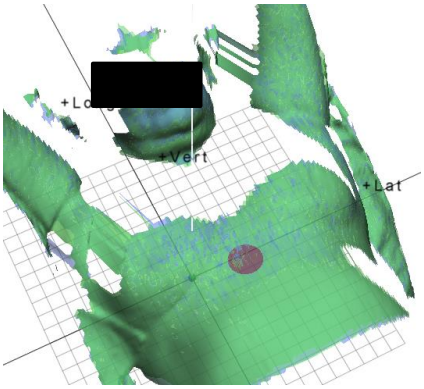
B.3 Treatment Guidelines

Behandlingsinstrukser udleveret til RTT'erne.

Behandlingsinstruks **CRAM**

MA 1548 (P) 30. marts 2016

CRAM
Behandlingsinstruks BU



Patient import til C-RAD

- Se instruksen "Behandlingsarm", der ligger i dette chartek.
- Se "import" instruksen, der ligger i dette chartek, for import af enten kontrolgruppen eller indsatsgruppen (gruppen er blevet valgt ovenfor).

Første fraktion (og boost fraktion).

- Se behandlings-instruksen for enten indsatsgruppen (s. 2) eller kontrolgruppen (s. 6).

Fra 2. fraktion:

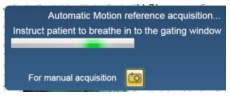
- Se instruksen for enten indsatsgruppen (s. 4) eller kontrolgruppen (s.8).

Behandlingsinstruks **CRAM**

MA 1548 (P) 30. marts 2016

Indsatsgruppe – 1. Fraktion

- Patienten vælges automatisk
- Sæt op efter laser
- Udfør delta couch
- **Noter** lejeparametre i skemaet.
- Juster på C-RAD kameraindstillinger og skanningsvolumenet ved tryk på  . Begge arme, hovedet og et stykke under processus xiphoideus skal inkluderes i skanningsvolumenet (hvis det ikke allerede er inkluderet) Tryk "ok". Se evt. side 10.
- Start setup i c-rad 
- Brug farvekortet til at justere patientens holdning (arme og hage). ***Noter*** *i skemaet*[1] *hvis I ændrer patientens holdning*.
- Udfør lejeflyt baseret på C-RAD
  - Overfør lejeparametre fra C-RAD til Varian Ved at trykke på C-RAD skærmen på  . Eller på fjernbetjeningen på  .
  - Dernæst trykkes på "auto enter" på Varian fjernbetjening for at udføre det ønskede lejeskift.
  - Se om de C-RAD lejeflyt falder til ro under 3 mm. Hvis ikke skal lejeflyt overføres fra C-RAD til Varian igen.
- Gå videre til gating modulet ved at trykke på  .
- **Noter** lejeparametre i skemaet.
- Juster evt. FSD (**VIGTIGT det sker efter tryk på**  !)
- **Noter** lejehøjden i skemaet efter evt. FSD justering
- Når baseline genberegnes vil følgende billede komme frem, det forsvinder automatisk når patienten tager sin første DIBH



- Fortsæt som normalt, og tag daglige billeder
- Behandling
- Afslut ved tryk på 
- Husk at **notere** side 3 i skemaet ved første fraktion.

Hvis patientens lejring fra CT skanningen ikke kan reproduceres, fx hvis der har været brugt en ring ved CT skanningen som ikke bruges ved behandlingen så skal der tages en ny reference når de daglige billeder er taget. Se side 14.

[1] Patientforløb samt behandlings-og undersøgelsesskema

Behandlingsinstruks **CRAM**

MA 1548 (P) 30. marts 2016

Oversigt: Indsatsgruppe – 1. Fraktion

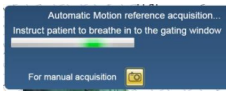
1. • LASER & DELTA COUCH
2. • NOTÉR LEJEPARAMETRE
3. 
4. • JUSTER KAMERA-INDSTILLINGER OG SKANVOLUMEN I C-RAD
5. 
6. • C-RAD SETUP (FARVEKORT + LEJEFLYT)
7. • Overfør og udfør lejeflyt fra C-RAD til Varian 
8. • NOTER C-RAD PATIENT-JUSTERING
9. 
10. • NOTÉR LEJEPARAMETRE
11. • AFLÆS OG JUSTER FSD
12. • NOTÉR LEJEHØJDEN
13. • DAGLIGE BILLEDER
14. • BEHANDLING
15. • NOTÉR PÅ SIDE 3 I SKEMAET[1]

[1] Patientforløb samt behandlings-og undersøgelsesskema

Behandlingsinstruks **CRAM**

MA 1548 (P) 30. marts 2016

Indsatsgruppe – Fra 2. fraktion:

- Patienten vælges automatisk
- Sæt op efter laser
- Udfør delta couch
- **Noter** lejeparametre i skemaet[1].
- Start setup i c-rad 
  - NB hvis den blå overflade ikke er tilfredsstillende – fx hvis den er meget hullet, prøv da at justere kameraindstillingerne ved at trykke på  og derefter på  . Når kameraet er blevet indstillet trykkes på "ok" og derefter på  . Se evt. side 10.
- Brug farvekortet til at justere patientens holdning (arme og hage). ***Noter** i skemaet hvis I ændrer patientens holdning*.
- Udfør lejeflyt baseret på C-RAD
  - Overfør lejeparametre fra C-RAD til Varian Ved at trykke på C-RAD skærmen på  . Eller på fjernbetjeningen på  .
  - Dernæst trykkes på "auto enter" på Varian fjernbetjening for at udføre det ønskede lejeskift.
  - Se om de C-RAD lejeflyt falder til ro under 3 mm. Hvis ikke skal lejeflyt overføres fra C-RAD til Varian igen.
- Gå videre til gating modulet ved at trykke på  .
- **Noter** lejeparametre i skemaet.
- Juster evt. FSD (**VIGTIGT det sker efter tryk på**  !)
- **Noter** lejehøjden i skemaet efter evt. FSD justering
- Når baseline genberegnes vil følgende billede komme frem, det forsvinder automatisk når patienten tager sin første DIBH 

- Tag CBCT ugentligt[2] - følg gældende instruks. **Noter** antal DIBHs under CBCT i skemaet. Der skal ikke matches på CBCT.
- Fortsæt som normalt, og tag daglige billeder
- Behandling
- Afslut ved tryk på 
- Husk at **notere** side 3 i skemaet[1] hvis der fx sker ændringer i patientens lejring, eller patienten får svært ved at blive gated.

[1] Patientforløb samt behandlings-og undersøgelsesskema
[2] CBCT ugentligt ved 2., 7., 12., 17. 22. fraktion. For boost fraktionen er det kun ved 2. boost fraktion

Hvis patientens lejring fra CT skanningen ikke kan reproduceres, fx hvis der har været brugt en ring ved CT skanningen som ikke bruges ved behandlingen så skal der tages en ny reference når de daglige billeder er taget. Se side 14.

Behandlingsinstruks **CRAM**

MA 1548 (P) 30. marts 2016

Oversigt: Indsatsgruppe – Fra 2. fraktion:

1. • LASER & DELTA COUCH
2. • NOTÉR LEJEPARAMETRE
3. 
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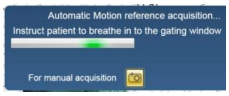
5. • Overfør og udfør lejeflyt fra C-RAD til Varian 
6. • NOTER C-RAD PATIENT-JUSTERING
7. 
8. • NOTÉR LEJEPARAMETRE
9. • AFLÆS OG JUSTER FSD
10. • NOTÉR LEJEHØJDEN
11. • UGENTLIG CBCT[2]
12. • NOTÉR ANTALLET AF DIBHS
13. • DAGLIGE BILLEDER
14. • BEHANDLING

[2] **CBCT ugentligt ved 2., 7., 12., 17. 22. fraktion. For boost fraktionen er det kun ved 2. boost fraktion**

Behandlingsinstruks **CRAM**

MA 1548 (P) 30. marts 2016

Kontrolgruppe – 1. Fraktion

- Patienten vælges automatisk
- Sæt op efter laser
- Udfør delta couch
- **Noter** lejeparametre i skemaet[1].
- Juster på C-RAD kameraindstillinger og skanningsvolumenet ved tryl på  .
  Begge arme, hovedet og et stykke under processus xiphoideus skal inkluderes i skanningsvolumenet (hvis det ikke allerede er inkluderet). Se evt. side 10.
- Start setup i c-rad 
- Vent et øjeblik på at den grønne proces bar bliver fyldt, så C-RAD kan nå at regne færdig
  - C-rad regner 
  - C-RAD er færdig med at regne 
- Tryk på  .
- Juster evt. FSD (**VIGTIGT det sker efter tryk på**  !)
- **Noter** lejehøjden i skemaet efter evt. FSD justering
- Når baseline genberegnes vil følgende billede komme frem, det forsvinder automatisk når patienten tager sin første DIBH 

- Fortsæt som normalt, og tag daglige billeder
- Behandling
- Afslut ved tryk på 
- Husk at **notere** side 3 i skemaet ved første fraktion.

[1] Patientforløb samt behandlings-og undersøgelsesskema

Hvis patientens lejring fra CT skanningen ikke kan reproduceres, fx hvis der har været brugt en ring ved CT skanningen som ikke bruges ved behandlingen så skal der tages en ny reference når de daglige billeder er taget. Se side 14.

Behandlingsinstruks **CRAM**

MA 1548 (P) 30. marts 2016

Oversigt: Kontrolgruppe – 1. Fraktion

1. • **LASER & DELTA COUCH**
2. • **NOTÉR LEJEPARAMETRE**
3. 
4. • **JUSTER KAMERA-INDSTILLINGER OG SKANVOLUMEN I C-RAD**
5. 
6. • **VENT PÅ C-RAD HAR REGNET FÆRDIG (GRØN PROCESSBAR FYLDT)**
7. 
8. • **AFLÆS OG JUSTER FSD**
9. • **NOTÉR LEJEHØJDEN**
10. • **DAGLIGE BILLEDER**
11. • **BEHANDLING**
12. • **NOTÉR PÅ SIDE 3 I SKEMAET**[1]

Behandlingsinstruks **CRAM**

MA 1548 (P) 30. marts 2016

Kontrolgruppe – Fra 2. Fraktion

- Patienten vælges automatisk
- Sæt op efter laser
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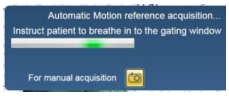
- Start setup i c-rad .
  - NB hvis den blå overflade ikke e  de – fx hvis den er meget hullet, prøv da at justere kameraindstillingerne ved at trykke på  og derefter på  . Når kameraet er blevet indstillet trykkes på "ok" og derefter på  . Se evt. side 10.
- Tryk på  .
- Vent et øjeblik på at den grønne proces bar bliver fyldt, så C-RAD kan nå at regne færdig
  - C-rad regner 
  - C-RAD er færdig med at regne 
- Juster evt. FSD (**VIGTIGT det sker efter tryk på**  !)
- **Noter** lejehøjden i skemaet efter evt. FSD justering
- Når baseline genberegnes vil følgende billede komme frem, det forsvinder automatisk når patienten tager sin første DIBH



- Tag CBCT[2] - følg gældende instruks. **Noter** antal DIBHs under CBCT i skemaet. Der skal ikke matches på CBCT.
- Fortsæt som normalt, og tag daglige billeder
- Behandling
- Afslut ved tryk på 
- Husk at notere side 3 i skemaet[1] hvis der fx sker ændringer i patientens lejring, eller patienten får svært ved at blive gated.

Behandlingsinstruks **CRAM**

MA 1548 (P) 30. marts 2016

Oversigt: Kontrolgruppe – Fra 2. fraktion

1. • LASER & DELTA COUCH
2. • NOTÉR LEJEPARAMETRE
3. 
4. • VENT PÅ C-RAD HAR REGNET FÆRDIG (GRØN PROCESSBAR FYLDT)
7. 
9. • AFLÆS OG JUSTER FSD
10. • NOTÉR LEJEHØJDEN
11. • UGENTLIG CBCT[2]
12. • NOTÉR ANTALLET AF DIBHS
13. • DAGLIGE BILLEDER
14. • BEHANDLING

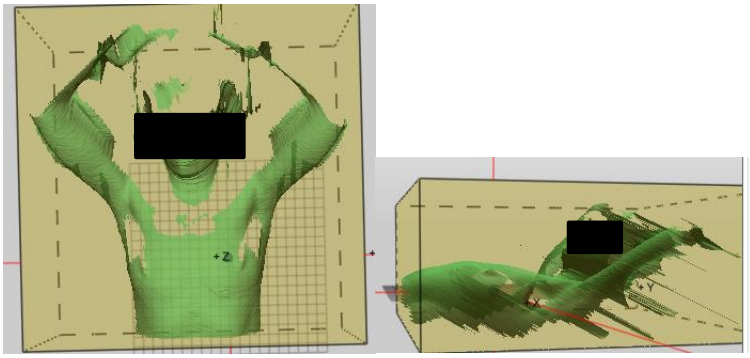
[2] **CBCT ugentligt ved 2., 7., 12., 17. 22. fraktion. For boost fraktionen er det kun ved 2. boost fraktion**

Behandlingsinstruks **CRAM**

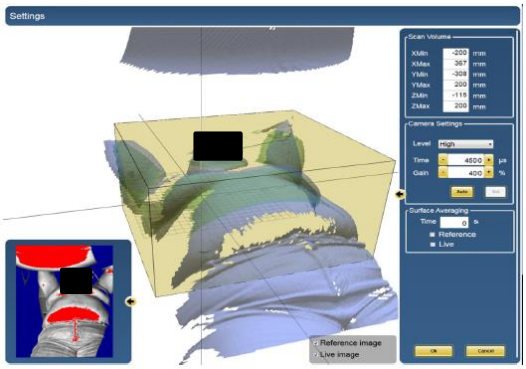
MA 1548 (P) 30. marts 2016

Skanningsvolumen

Hovedet og armene er inkluderet i overfladeskanningen, samt et stykke under processus xiphoideus. Se eksempler nedenfor.



Kameraindstillinger



Den grønne overflade er fra CT skanningen, mens den blå er live-overfladen(den vi ser nu her).

Patientens body skal være blå, især vigtigt der hvor primærpunktet forventes at være placeret, samt ved armene. Ses tydeligt hvis man fjerner fluebenet for *reference image.*

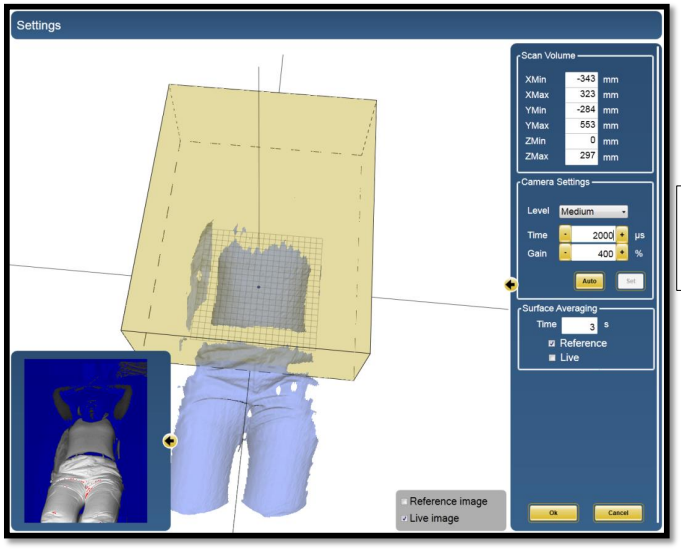
Start med at trykke på ”**auto**”. Hvis den **blå body** ikke er tilfredsstillende kan der ændres på værdien **"Time"** og/eller **"Gain"** som findes i boksen **"Camera settings"**. Normalt er det nok at ændre på **"Time"**. Hvis **"Gain"** ændres anbefales det normalt ikke at vælge en værdi større end 400%.

Behandlingsinstruks **CRAM**

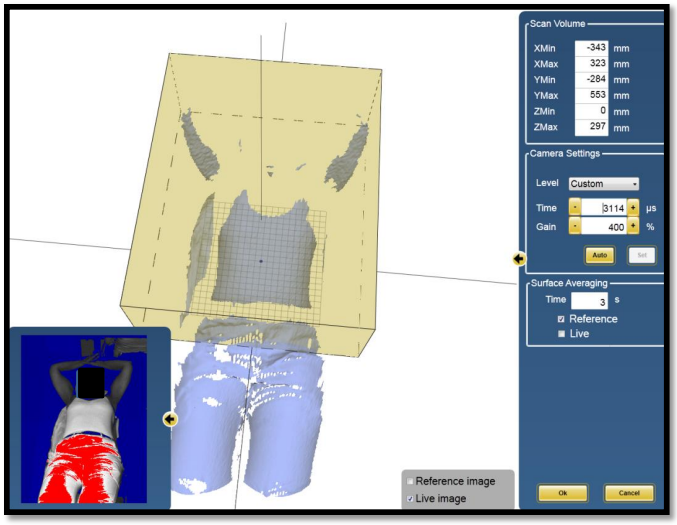
MA 1548 (P) 30. marts 2016

- Hvis der er huller eller områder der mangler i body vil "**Time**" normalt skulle øges.
- Hvis der er røde områder i sort/hvid billedet nederst til venstre, kan disse områder være svære at se. For at justere for røde områder skal en mindre "**Time**" vælges. Dette kan fx ses på det nederst af maven i figuren ovenfor – hvis dette område skal være optimalt dækket kræves det at "Time" reduceres.
    - Dette vil dog oftest ske på bekostning af et andet område bliver mindre synligt – så det er en balance gang.
- Hvis body stadig ikke er tilfredsstillende kan "**Gain**" øges, normalt til max. 800%.

<u>Eksempler kan ses på næste side</u>

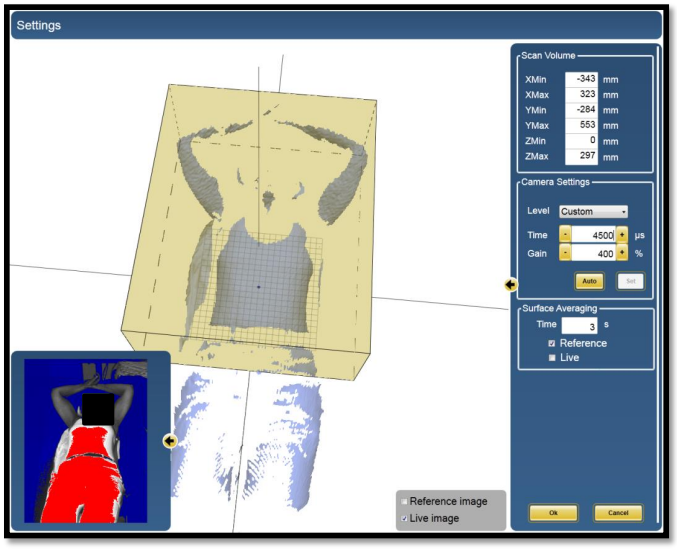


Kameraet kan ikke se armene. Prøver at skrue op for "Time".



”Time” skruet op og man kan nu se det nederste af armene.

Prøver at skrue lidt mere op for ”Time”.



”Time” skruet op og man kan nu se hele armen.

Der er dog en del røde områder ved omkring stedet hvor primærpunktet forventes at være. Så indstillingen ovenfor (Time = 3114) er mest optimal.

Behandlingsinstruks **CRAM**

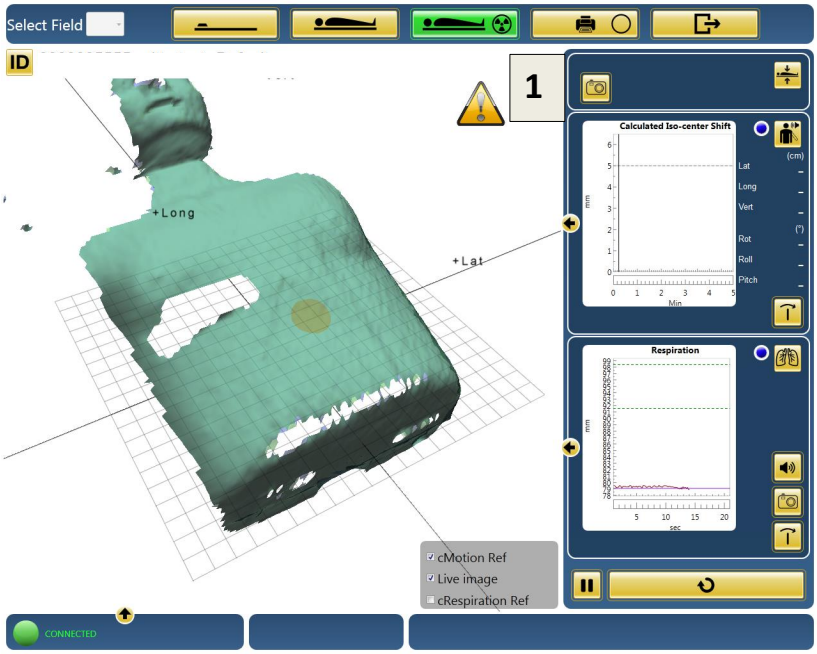
MA 1548 (P) 30. marts 2016

Ny C-RAD reference efter daglige billeder

Referencen skal tages efter de daglige billeder, inden behandlingen gives. Dette gøres på følgende måde.

1. Tryk på kameraet  i den øverste højre del af C-RAD skærmen:

   - Det er vigtigt det ikke er gating kamereaet nederst der bliver trykket på. Hvis der ved en fejl trykkes på gating kameraet, vælges "cancel". Og der trykket på det øverste kamera.

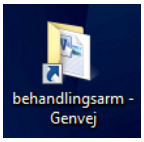


2. Der trykket "Yes", hvorved der bliver lavet en ny reference

Instruks til behandlingsarm **CRAM**

MA 1548 (P) 30-03-2016

1) På computerens skrivebord ligger en genvej til dokumentet som skal bruges:



Hvis genvejen ikke kan findes kan man alternativ gå ind på p-drevet ved at bruge følgende sti:

P:\Onkologisk Afdeling R\CRAD\CRAM\behandlingsarm

2) Åben dokumentet "*Behandlingsarm*", der ligger i mappen.
3) I dokumentet skrives dato, tidspunkt og behandlingsapparat. Yderst til højre kan behandlingsarmen ses for den pågælgende patient

Patientnummer	Dato	Tidspunkt	Behandlingsapparat	Behandlingsarm
1	23/1-16	10.30	gefion	Kontrolgruppe
2				Indsatsgruppe
3				Kontrolgruppe
4				Indsatsgruppe

Når en patient kommer der skal indgå i protokollen vil jeg altså indtaste:

Patientnummer	Dato	Tidspunkt	Behandlingsapparat	Behandlingsarm
1	23/1-16	10.30	Gefion	Kontrolgruppe
2	11/2-16	11.15	Thor	Indsatsgruppe
3				Kontrolgruppe

Patienten tilhører altså indsatsgruppen og har patientnummer 2.

4. **HUSK** at gemme dokumentet og skrive behandlingsarm og patientnummer i "behandlings-og undersøgelsesskemaet".

Importinstruks **CRAM**

MA 1548 (P) 30. Marts 2016

Kontrolgruppe

Klargøring af C-Rad, efter CT planlægning og inden opstart af strålebehandling.

På C-Rad skærmen trykkes på ikonet  .

1. Tryk på fanbladet "*Import"* øverst oppe på skærm billedet.
2. Marker patientens navn.
3. Tryk på Open nederst til højre i vinduet.

Hvis patientens navn ikke står på listen, så tjek at Directory er sat til:" \\rghheariaimg001\CRad". Tryk dernæst på ikonet  .

Hvis patienten stadig ikke er på listen, skal patienten eksporteres fra Eclipse igen. Kontakt Fysiker på 82 451.

Hvis en patient skal have boost eller bilateral strålebehandling, vil patientens navn fremkomme 2 gange. Planerne skal importeres en ad gangen.

Importering af C-rad planen

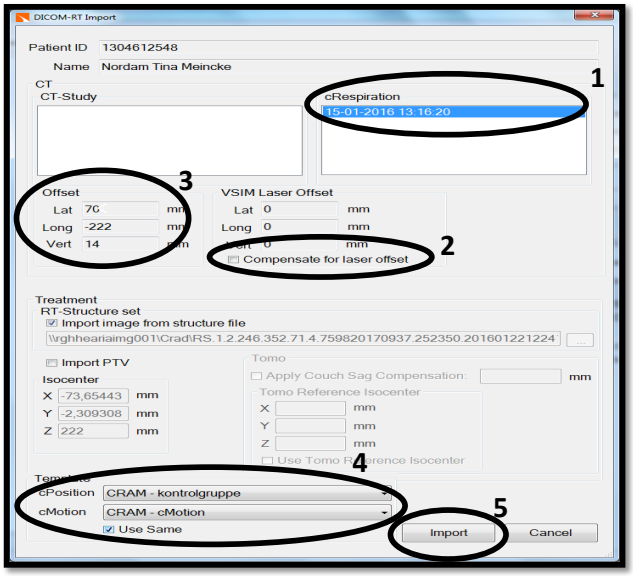
1. I vinduet cRespiration, markeres gating referencen fra CT scanneren (dato og tid) så den bliver blå.

OBS Hvis der er 2, skal vi kontakte scanner personalet for at få fjernet den der ikke skal bruges. Kontakt til BF 89 230. Hvis den forkerte reference bliver brugt, kan det betyde at gating punktet og gating vinduet er forkert. Grunden er at patienten er blevet scannet flere gange.

2. Fjern fluebenet fra "*Compensate for laser offset*"
3. Tjek Offset. Der skal være tal. Svarer til delta couch.
4. Under ”cPosition” vælges enten ”CRAM - kontrolgruppe” på listen. Under ”cMotion” vælges ”CRAM-cMotion.
5. Tryk på **Import**

Importinstruks **CRAM**

MA 1548 (P) 30. Marts 2016



Kontrolgruppe

Der kan nogle gange komme en dialog boks frem "*Update patient*". Hvor patient navn og fødselsdag opdateres. Det har ingen betydning og derfor accepteres dette med Ja (eller Yes).

I dialog boksen "*C-RAD c4D - Herlev*"

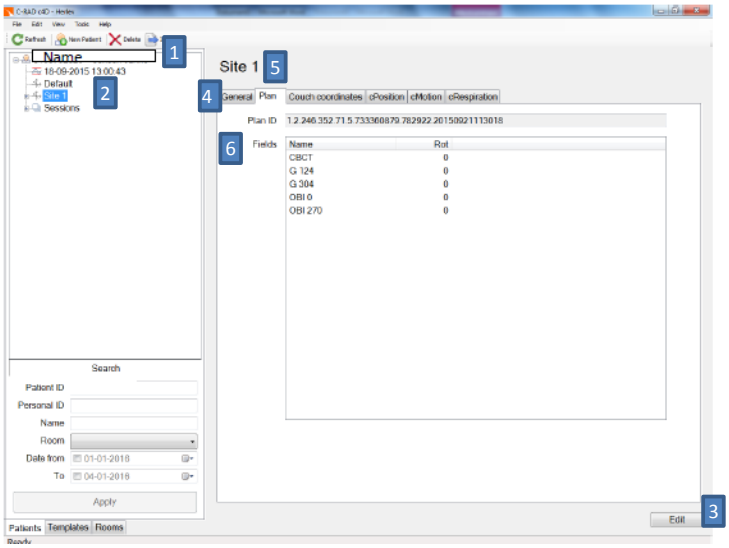
1. Tryk på ***Edit***. Det er nu muligt at arbejde i planen.
2. I dialogboksen "*Edit Patient*" under ***Room*** vælges eller ændres behandlingslokalet ud fra drop down listen.
3. Under fanebladet "*Settings*" skal der være flueben alle steder (*Use cPosition for setup*", "*Use cMotion for treatment*" og "Use cRespiration for treatment".
4. Tryk ***OK***

Tjek planens indstillinger

1. Find patienten i venstre kolonne. Tryk på "**+**" ud for patientens navn. Man kan nu se indholdet i patientens plan.
2. Tryk på "*Site 1*" (markeres blå)
3. Tryk på **Edit** og dialogboksen "*EDIT site*" åbner.
4. Tryk på fanebladet "*General*". Catalyst Camera settings skal være den samme som Sentinel kameraets. Sentinel kameraets indstilling findes under fanebladet "*cRespiration*". Der kan f.eks. står Medium eller

High. Evt. ændring udføres under fanebladet "General" under vinduet "*Catalyst Camera Settings*" i drop down listen: "*Sensitivity*".

5. Tryk på fanebladet "*Plan*".
6. Tjek feltnavnene under "*Fields*" stemmer overens med behandlingsplanen i RT-Chart. Der SKAL ud for hvert felt navn, under "Rot", stå 0. Ved mangel kald fysiker 82 451.
7. Tryk **OK**

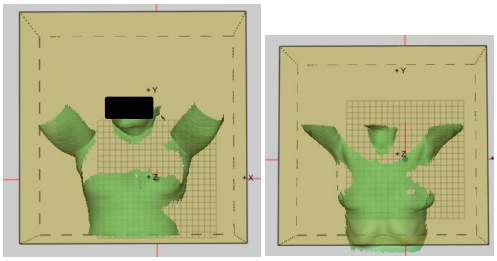


Importinstruks **CRAM**

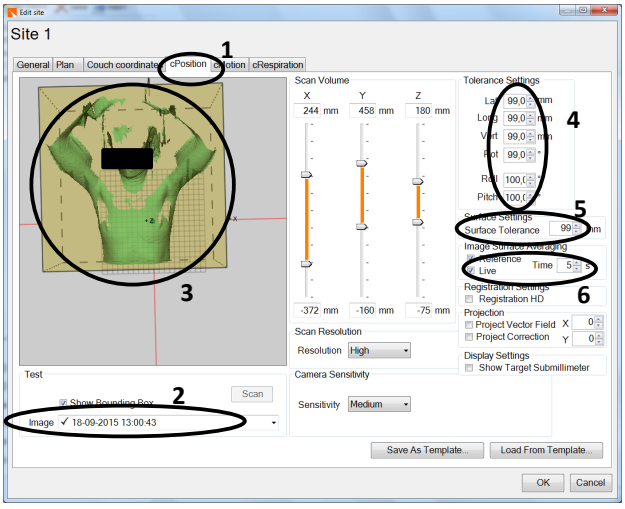
MA 1548 (P) 30. Marts 2016

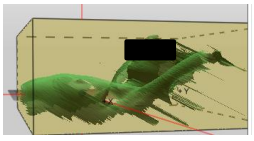
Juster skanningsvolumenet

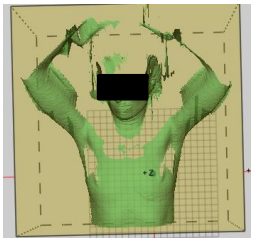
1. Tryk på fanebladet ”cPosition” og tryk på ”edit”.
2. Vælg Sentinel referencen fra CT skanningen
3. Juster skanningsvolumenet så det inkluderer hovedet og begge armene, og et stykke under processus xiphoideus. Dette gøres ved at ”strække” i kassen med musen.
    a. Hvis armene ikke er inkluderet i skanningen som vises, kan det være fordi gantryet har skygget. I så fald udvides boksen ekstra i den X og Y retningen for at sikre armene kan være med. Se eksempler lige nedenfor.



4. Under tolerance settings skal der står ”99” eller ”100” alle steder.
5. Surface tolerance skal være sat til 99mm”
6. Surface averaging skal være sat til ”5s”.





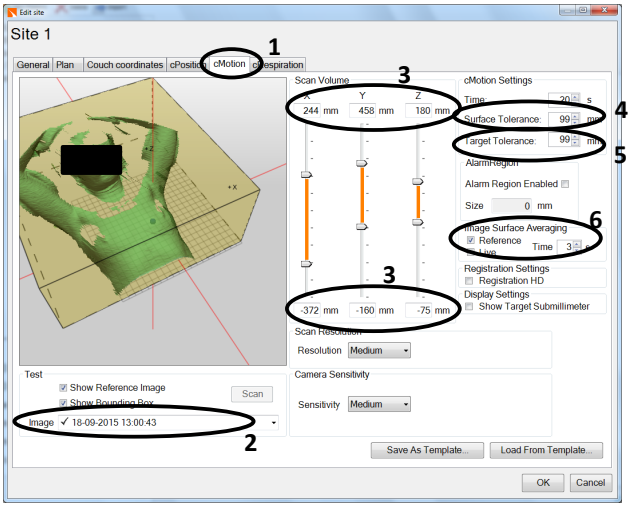


Importinstruks **CRAM**

MA 1548 (P) 30. Marts 2016

Det samme gøres for cMotion:

1. Tryk på fanebladet ”cMotion”.
2. Vælg Sentinel referencen fra CT skanningen . ✓
3. Juster skanningsvolumenet ved at taste ind under X, Y og Z. Det skal være samme værdier som under cPosition.
4. Surface tolerance = 99 mm
5. Target tolerance = 99mm
6. Surface averaging skal være sat til ”3s”.
7. Tryk ”OK”



Tjek Video coaching indstillingen

1. Find den aktuelle patient i listen over patienter (til venstre i skærm billedet).
2. Tryk på "**+**" ud for "*Site 1”*
3. Marker 3. linje (blå): " √ *dato + tid (fra patientens terapi scanning)*"
4. Tryk på Fanebladet "*Settings". Se* under rubrikken "*Coaching*" om der er et flueben(√) udfor "*Video*". Hvis indstillingen ikke er i orden kan patienten ikke se noget i brillerne.
5. Skal der justeres: Tryk på **EDIT**. Dialogboksen: "*Edit cRespiration reference*" kommer frem. Tryk på fanebladet "*Settings"* og sæt et flueben (√) i *"Video".*
6. Tryk **OK** for at gemme.
7. Tryk på "**+**" ud for patientens navn for at lukke planen.

C-Rad planen er nu klar til strålebehandling med DIBH.

Under **View** knappen tryk på "*Switch to Clinical mode.....".*

Importinstruks **CRAM**

MA 1548 (P) 30. Marts 2016

Ændring i strålebehandlingsplanen

Enhver form for ændring i behandlingsplanen (dog ikke set-up note) vil medføre en ny plan identitet i *Eclipse*. Det betyder, at C-Rad programmet ikke kan genkende planen. Der vil på C-rad skærmen stå "*Unknown Patient*", selv om det er en patient, som skal behandles med C-Rad.

- Fysikerne skal, når de ændrer noget i en behandlingsplan eksportere C-rad planen igen.
- Fysikerne skal skrive det på rapportarket.
- BU skal oprette planen i C-Rad igen.

Importinstruks **CRAM**

MA 1548 (P) 30. Marts 2016

Indsatsgruppe

Klargøring af C-Rad, efter CT planlægning og inden opstart af strålebehandling.

På C-Rad skærmen trykkes på ikonet  .

1. Tryk på fanbladet "*Import*" øverst oppe på skærm billedet.
2. Marker patientens navn.
3. Tryk på Open nederst til højre i vinduet.

Hvis patientens navn ikke står på listen, så tjek at Directory er sat til:" \\rghheariaimg001\CRad". Tryk dernæst på ikonet  .

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Hvis en patient skal have boost eller bilateral strålebehandling, vil patientens navn fremkomme 2 gange. Planerne skal importeres en ad gangen.

Importering af C-rad planen

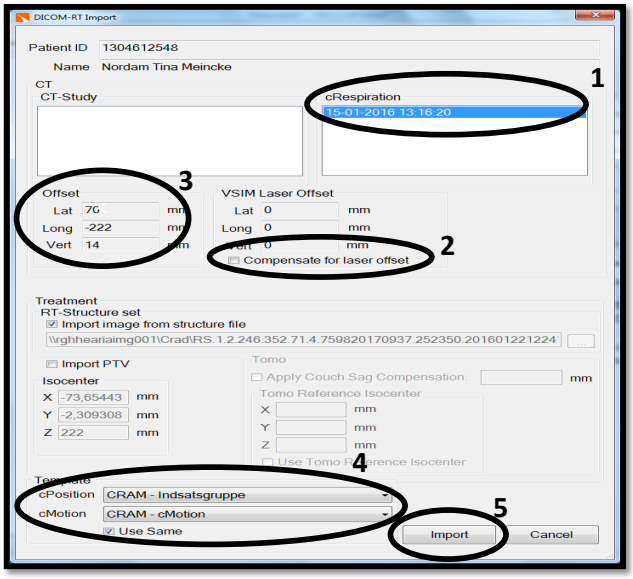
1. I vinduet cRespiration, markeres gating referencen fra CT scanneren (dato og tid) så den bliver blå.

OBS Hvis der er 2, skal vi kontakte scanner personalet for at få fjernet den der ikke skal bruges. Kontakt til BF 89 230. Hvis den forkerte reference bliver brugt, kan det betyde at gating punktet og gating vinduet er forkert. Grunden er at patienten er blevet scannet flere gange.

2. Fjern fluebenet fra "*Compensate for laser offset*"
3. Tjek Offset. Der skal være tal. Svarer til delta couch.
4. Under ”cPosition” vælges enten ”CRAM – Indsatsgruppe” på listen. Under ”cMotion” vælges ”CRAM-cMotion”.
5. Tryk på **Import**

Importinstruks **CRAM**

MA 1548 (P) 30. Marts 2016



Indsatsgruppe

Der kan nogle gange komme en dialog boks frem "*Update patient*". Hvor patient navn og fødselsdag opdateres. Det har ingen betydning og derfor accepteres dette med Ja (eller Yes).

I dialog boksen "*C-RAD c4D - Herlev*"

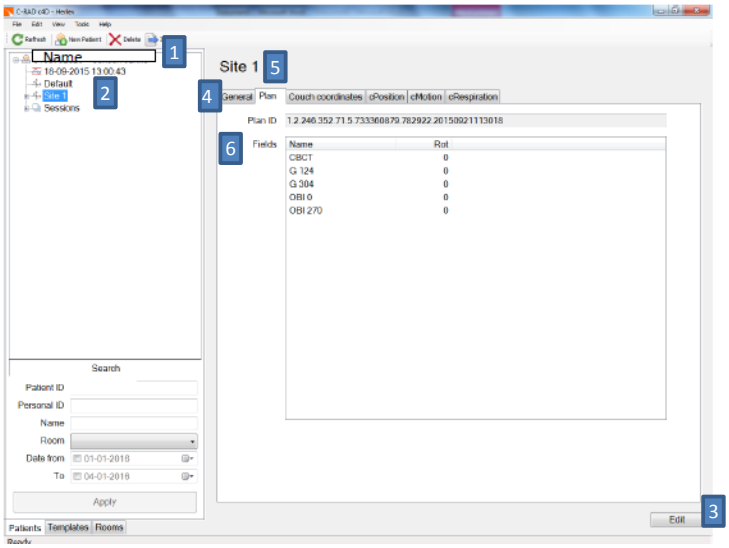
1. Tryk på ***Edit***. Det er nu muligt at arbejde i planen.
2. I dialogboksen "*Edit Patient*" under ***Room*** vælges eller ændres behandlingslokalet ud fra drop down listen.
3. Under fanebladet "*Settings*" skal der være flueben alle steder (*Use cPosition for setup*", "*Use cMotion for treatment*" og "Use cRespiration for treatment".
4. Tryk ***OK***

Tjek planens indstillinger

1. Find patienten i venstre kolonne. Tryk på "**+**" ud for patientens navn. Man kan nu se indholdet i patientens plan.
2. Tryk på "*Site 1"* (markeres blå)
3. Tryk på **Edit** og dialogboksen "*EDIT site"* åbner.
4. Tryk på fanebladet "*General"*. Catalyst Camera settings skal være den samme som Sentinel kameraets. Sentinel kameraets indstilling findes under fanebladet "*cRespiration*". Der kan f.eks. står Medium eller

High. Evt. ændring udføres under fanebladet "General" under vinduet "*Catalyst Camera Settings*" i drop down listen: "*Sensitivity*".

5. Tryk på fanebladet "*Plan*".
6. Tjek feltnavnene under "*Fields*" stemmer overens med behandlingsplanen i RT-Chart. Der SKAL ud for hvert felt navn, under "Rot", stå 0. Ved mangel kald fysiker 82 451.
7. Tryk **OK**

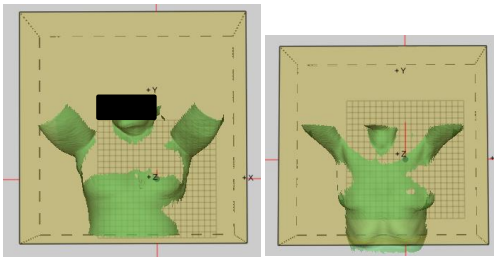


Importinstruks **CRAM**

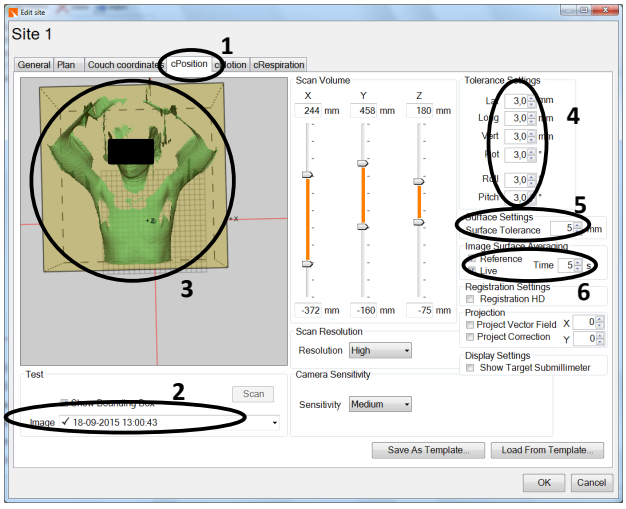
MA 1548 (P) 30. Marts 2016

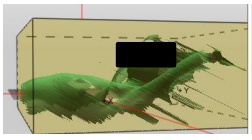
Juster skanningsvolumenet

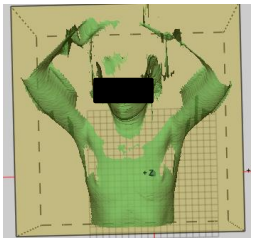
1. Tryk på fanebladet ”cPosition” og tryk på ”edit”.
2. Vælg Sentinel referencen fra CT skanningen
3. Juster skanningsvolumenet så det inkluderer hovedet og begge armene, og et stykke under processus xiphoideus. Dette gøres ved at ”strække” i kassen med musen.
    a. Hvis armene ikke er inkluderet i skanningen som vises, kan det være fordi gantryet har skygget. I så fald udvides boksen ekstra i den X og Y retningen for at sikre armene kan være med. Se eksempler lige nedenfor.



4. Under tolerance settings skal der står ”3,0” alle steder.
5. Surface tolerance skal være sat til ”5 mm”
6. Surface averaging skal være sat til ”5s”.





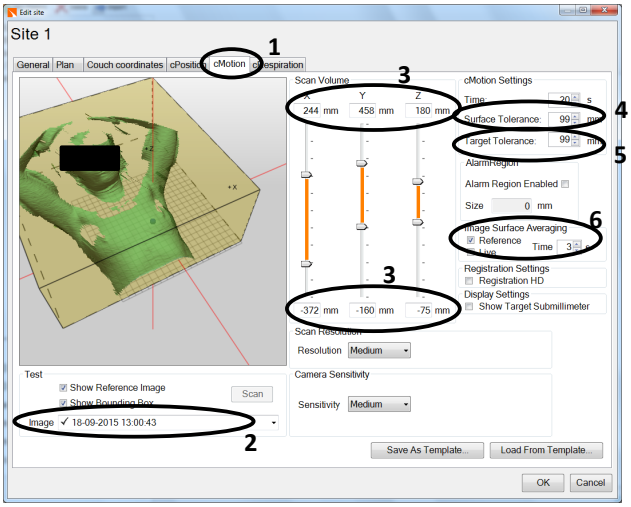


Importinstruks **CRAM**

MA 1548 (P) 30. Marts 2016

Det samme gøres for cMotion:

1. Tryk på fanebladet ”cMotion”.
2. Vælg Sentinel referencen fra CT skanningen . ✓
3. Juster skanningsvolumenet ved at taste ind under X, Y og Z. Det skal være samme værdier som under cPosition.
4. Surface tolerance = 99 mm
5. Target tolerance = 99mm
6. Surface averaging skal være sat til ”3s”.
7. Tryk ”OK”



Tjek Video coaching indstillingen

1. Find den aktuelle patient i listen over patienter (til venstre i skærm billedet).
2. Tryk på "**+**" ud for "*Site 1”*
3. Marker 3. linje (blå): " *√‾dato + tid (fra patientens terapi scanning)*"
4. Tryk på Fanebladet "*Settings". Se* under rubrikken "*Coaching*" om der er et flueben(√) udfor "*Video*". Hvis indstillingen ikke er i orden kan patienten ikke se noget i brillerne.
5. Skal der justeres: Tryk på **EDIT**. Dialogboksen: "*Edit cRespiration reference*" kommer frem. Tryk på fanebladet "*Settings"* og sæt et flueben (√) i *"Video".*
6. Tryk **OK** for at gemme.
7. Tryk på "**+**" ud for patientens navn for at lukke planen.

C-Rad planen er nu klar til strålebehandling med DIBH.

Under **View** knappen tryk på "*Switch to Clinical mode.....".*

Importinstruks **CRAM**

MA 1548 (P) 30. Marts 2016

Ændring i stråle behandlingsplanen

Enhver form for ændring i behandlingsplanen (dog ikke set-up note) vil medføre en ny plan identitet i *Eclipse*. Det betyder, at C-Rad programmet ikke kan genkende planen. Der vil på C-rad skærmen stå "*Unknown Patient*", selv om det er en patient, som skal behandles med C-Rad.

- Fysikerne skal, når de ændrer noget i en behandlingsplan eksportere C-rad planen igen.
- Fysikerne skal skrive det på rapportarket.
- BU skal oprette planen i C-Rad igen.

B.4 Treatment Schedule Handout

Behandlings- og udnersøgelsesskema som blev udfyldt da planlægnings CT skanningen blev lavet, og til og med den endelige behandlingsfraktion.

Patientforløb samt Behandlings-og undersøgelsesskema *(ligges i strålemappen)* 27-01-2018
CRAM-protokol: MA 1548 (P) Protokolansvarlig: Susanne Bekke (89365)

Patientforløb: CRAM-protokol *Medlemmer af projektgruppen:* Susanne Nørring Bekke (89365) [Projektansvarlig] Faisal Mahmood (89518)	**Patient label**

Handling	Dato	Initialer
BF – ved samtalen i Mould • Patienten informeres om protokollen, jf. "Mundtlig information om CRAM". • Patienten får udleveret relevante dokumenter (Deltagerinformation, Forsøgspersoners rettigheder, Samtykkeerklæringen). Dokumenterne ligger i dueslaget ved Mould.		
Hvis patienten indvilger i at deltage i forsøget, og ikke ønsker betænkningstid: • Samtykkeerklæringen underskrives og ligges i dueslaget ved Mould. En kopi gives til patienten og en kopi ligges i strålemappen. • CRAM skrives på forsiden af strålemappen og i det elektroniske rapportark. • Arket (Dagsoversigt til sek/vis) til sekundær visitation udfyldes.		
Hvis patienten ønsker betænkningstid: • Patienten får tilbudt selv at ringe op dagen efter (Susanne [3868 9365] eller Faisal [3868 9518]), hvor patienten evt. får nærmere information om protokollen og patienten melder ud om hun ønsker at deltage i protokollen. • **Husk at ligge en samtykkeerklæring i strålemappen med underskrift fra den der har givet informationen til patienten i Mould.**		
BF – ved CT skanningen • "Behandlings-og undersøgelsesskema" udfyldes.		
Patienten ringer op • Patienten ringer op til Susanne eller Faisal, for evt. uddybende information og for at fortælle at patienten ønsker at deltage i protokollen. Ved deltagelse: Sek/vis og BU (Susanne L eller Annbritt) får besked.		
Sekundær visitation • Får besked om patienter via arket "*Dagsoversigt til sek/vis*" fra BF, og om patienterne allerede har underskrevet samtykke. Behandlingen skal foregå i dagvagten.		
BU – import • Planen importeres til C-RAD efter CRAM instruksen.		
BU – Faisal eller Susanne ringer med besked om mundtligt samtykke • CRAM skrives på forsiden af strålemappen og i det elektroniske rapportark		
BU – ved Strålebehandlingen • **Fraktion 1:** Der skal forefindes dokumentation for patientens samtykke til at deltage (samtykkeerklæring). Hvis patienten kun har givet mundtligt tilsagn om at deltage skal samtykkeerklæringen underskrives og ligges i dueslaget ved Mould. En kopi gives til patienten og en kopi ligges i strålemappen. Det sikres at der står CRAM på strålemappens forside og i det elektroniske rapportark.		
Hvis patienten har ønsket betænkningstid, og først giver samtykke ved fraktion 1: • Sek/vis skal hurtigst muligt have besked om patienten deltager i eller ej.		
• For patienter der har givet samtykke skal behandlingsarmen vælges ud fra listen på p-drevet (*P:\Onkologisk Afdeling R\CRAD\CRAM\liste)*, se evt. instruks. Det er vigtigt listen gemmes når patienten er blevet inkluderet.		
• "Behandlings- og undersøgelsesskema" udfyldes dagligt		
Sidste fraktion: Når patienten afsluttes ved BU, afleveres arket til Susanne Lind ved specialistkontoret.		

Når patienten afsluttes ved BU afleveres arket til Susanne Lind i dueslaget på specialistkontoret

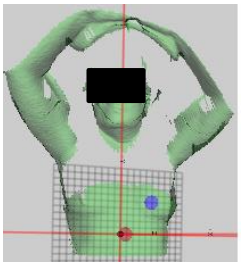
NB der tages CBCT ved 2., 7., 12., 17., 22. fraktion. Og ved 2. boost fraktion.

Patientforløb samt Behandlings-og undersøgelsesskema *(ligges i strålemappen)* 27-01-2018
CRAM-protokol: MA 1548 (P) Protokolansvarlig: Susanne Bekke (89365)

Behandlingsforberedende enhed

Patient Label

	TJEK ✓
Arme og hoved er inkluderet I C-RAD overfladeskanningen (se billedet)	



	JA	NEJ
Er primær punktet placeret ved sternum lige over processus xiphoideus?		
Hvis **nej,** hvorfor:		
Ikke noget signal ved processus xiphoideus		
Signalet er dårligt		
Signalet forsvinder under DIBH		
Maven skygger for primær punktet		
Beskriv evt. anden årsag til den nye placering:		
Har patienten svært ved at udføre DIBH?		
Har patienten svært ved at ligge med armene oppe?		
Evt. kommentarer		

Når patienten afsluttes ved BU afleveres arket til Susanne Lind i dueslaget på specialistkontoret

NB der tages CBCT ved 2., 7., 12., 17., 22. fraktion. Og ved 2. boost fraktion.

Patientforløb samt Behandlings-og undersøgelsesskema *(ligges i strålemappen)* 27-01-2018
CRAM-protokol: MA 1548 (P) Protokolansvarlig: Susanne Bekke (89365)

Behandlingsudførende enhed

Patient Label	Behandlingsarm (sæt kryds)	
	Kontrolgruppe (ingen positionering med C-RAD)	**Indsatsgruppe** (positionering med C-RAD)
	Patientnummer (fra arket med behandlingsarmen)	

	JA	**NEJ**	Evt. kommentar
Har patienten svært ved at udføre DIBH?			
Er patienten svær at lejre?			
Har i flyttet på gating punktet?			
Har i måtte ændre på patientens opstilling? Fx hvis patienten ikke kan have begge arme oppe, ringen er fjernet, eller lignende.			
Har i ændret på kameraindstillinger (time/gain) for at få en bedre overfladeskanning?			

Ovenstående tabel udfyldes primært ved første fraktion

Eventuelle gennerelle kommentarer:

Fraktion	**Kommentar**

OBS! HUSK at udfylde de næste sider ved hver fraktion!

Når patienten afsluttes ved BU afleveres arket til Susanne Lind i dueslaget på specialistkontoret

NB der tages CBCT ved 2., 7., 12., 17., 22. fraktion. Og ved 2. boost fraktion.

Patientforløb samt Behandlings-og undersøgelsesskema *(ligges i strålemappen)* 27-01-2018

CRAM-protokol: MA 1548 (P) Protokolansvarlig: Susanne Bekke (89365)

Patient Label	Behandlingsarm (sæt kryds)	
	Kontrolgruppe (ingen positionering med C-RAD)	**Indsatsgruppe** (positionering med C-RAD)

Kontrolgruppe: Her bliver positionering med C-RAD ikke brugt til at justere på patientens holdning, eller til at flytte på lejet. Overfladeskanninger bliver stadig gemt i C-RAD, og CBCT udføres ugentligt. *I skemaet nedenfor noteres **der** ikke noget ud for ændring i holdning og flyttet leje efter C-RADs analyse, dvs. det er kun de grå kolonner der udfyldes.*

Indsatsgruppe: Positionering med C-RAD bliver brugt til at justere på patientens holdning og til at lave evt. leje justeringer. Der udføres CBCT ugentligt. *I skemaet nedenfor noteres der alle steder.*

Fraktion	Har i ændret patientens **holdning** efter C-RAD? Fx armens placering		Noter lejeposition før lejet er blevet flyttet med på baggrund af C-RADs analyse.			Lejeposition lige **før** evt. FSD justering (Efter evt. C-RAD lejeflyt)			Lejehøjden **efter** evt. FSD justering (før billedtagning)	Hvor mange DIBHs krævede CBCT?
	JA	**NEJ**	**LAT**	**LNG**	**VRT**	**LAT**	**LNG**	**VRT**		
1										
2										
3										
4										
5										
6										
7										
8										
9										
10										
11										
12										
13										
14										

Når patienten afsluttes ved BU afleveres arket til Susanne Lind i dueslaget på specialistkontoret

NB der tages CBCT ved 2., 7., 12., 17., 22. fraktion. Og ved 2. boost fraktion.

Patientforløb samt Behandlings-og undersøgelsesskema *(ligges i strålemappen)* 27-01-2018
CRAM-protokol: MA 1548 (P) Protokolansvarlig: Susanne Bekke (89365)

Patient Label	Behandlingsarm (sæt kryds)	
	Kontrolgruppe (ingen positionering med C-RAD)	**Indsatsgruppe** (positionering med C-RAD)

Fraktion	Har i ændret patientens **holdning** efter C-RAD? Fx armens placering		Noter lejeposition før lejet er blevet flyttet med på baggrund af C-RADs analyse.			Lejeposition lige **før** evt. FSD justering (Efter evt. C-RAD lejeflyt)			Lejehøjden **efter** evt. FSD justering (før billedtagning)	Hvor mange DIBHs krævede CBCT?
	JA	**NEJ**	**LAT**	**LNG**	**VRT**	**LAT**	**LNG**	**VRT**		
15										
16										
17										
18										
19										
20										
21										
22										
23										
24										
25										

Når patienten afsluttes ved BU afleveres arket til Susanne Lind i dueslaget på specialistkontoret

NB der tages CBCT ved 2., 7., 12., 17., 22. fraktion. Og ved 2. boost fraktion.

Patientforløb samt Behandlings-og undersøgelsesskema *(ligges i strålemappen)* 27-01-2018

CRAM-protokol: MA 1548 (P) Protokolansvarlig: Susanne Bekke (89365)

Patient Label	Behandlingsarm (sæt kryds)	
	Kontrolgruppe (ingen positionering med C-RAD)	**Indsatsgruppe** (positionering med C-RAD)

For Boost-behandlingen

Fraktion	Har i ændret patientens **holdning** efter C-RAD? Fx armens placering		Noter lejeposition før lejet er blevet flyttet med på baggrund af C-RADs analyse.			Lejeposition lige **før** evt. FSD justering (Efter evt. C-RAD lejeflyt)			Lejehøjden **efter** evt. FSD justering (før billedtagning)	Hvor mange DIBHs krævede CBCT?
	JA	**NEJ**	**LAT**	**LNG**	**VRT**	**LAT**	**LNG**	**VRT**		
1										
2										
3										
4										
5										
6										
7										
8										

Når patienten afsluttes ved BU afleveres arket til Susanne Lind i dueslaget på specialistkontoret

NB der tages CBCT ved 2., 7., 12., 17., 22. fraktion. Og ved 2. boost fraktion.

Papers

PAPER

No Indications of Improvement in kV-MV Based Setup Using Optical Surface Scanning for Arm Posture Correction in Breast Radiotherapy

No indications of improvement in kV-MV based setup using optical surface scanning for arm posture correction in breast radiotherapy

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Abstract

Background and Purpose: It was investigated whether arm posture correction (APC) can lead to improved kV-MV based setup in breast radiotherapy. Further, the setup error based on laser, surface and planar kV-MV was compared.

Materials and Methods: Forty patients were included, 19 with APC using an optical surface scanning system. The potential treatment position was extracted using the different setup methods. The translational setup errors were evaluated using cone beam computed tomography (CBCT) and kV-MV as ground truth, while rotations were evaluated using CBCT.

Results: The median error vector length ($|\mathbf{\Delta}|$) from kV-MV based setup was not significantly different with or without APC. The median $|\mathbf{\Delta}|$ from surface based setup using the full surface ROI (navel to above the head) was significantly lower compared to setup based on laser and surface using the ROI from the target breast or both breasts.

Conclusion: No indications of improved kV-MV based setup with APC. However, APC was needed in 86 % of the fractions, suggesting that the clavicle position, used to guide kV-MV based setup, is insensitive to arm posture variation. The study suggests that surface based setup can be used for initial setup, but target position should be verified using e.g. kV-MV.

1. Introduction

Radiotherapy is used in breast cancer to reduce the risk of both local cancer recurrence and breast cancer death [1]. In radiotherapy it is crucial that patient geometry is reproduced accurately at each fraction. The initial setup is commonly guided by tattoo marks and in-room lasers (laser based setup), and can be verified using planar megavoltage (MV) field imaging, planar kilovoltage (kV) imaging and/or cone beam computed tomography (CBCT). Additional patient positioning with an optical surface scanning (OS) system, not utilizing ionising radiation, can be applied. An OS-system is capable of detecting deviations between a current surface and an earlier recorded reference surface. By comparing these surfaces, the system can provide corrections for patient posture, e.g. arm posture, and couch adjustments in six degrees of freedom to move the patient to the planned isocenter position prior to treatment. The OS-system have been shown to be more accurate than laser based setup [2–4], and shown potential to reduce the number of days with need for position verification using imaging based on ionizing radiation [5–7]. Changes in arm posture from day to day despite the use of breast board have previously been observed using an OS-system [3,8], but the effect of correcting them have not been studied. Arm position variation can lead to deformation of the breast tissue and have been shown to give rise to position variation of the lateral clavicle [9]. The latter could lead to inconsistencies when performing daily 2D image guided radiotherapy as the clavicle is often used as guideline for the registration process [10].

In this prospective study we investigated if arm posture correction using an OS-system improves setup based on kV-MV. Further we compared the setup error based on laser, kV-MV and surface using CBCT as the ground truth. Three different regions of interest (ROIs), one covering the surface area from approximately the navel to above the head, one covering both breasts, and one covering the target breast were investigated for surface based setup.

2. Materials & Methods

2.1 Patients

Forty left-sided breast cancer patients without lymph node involvement scheduled for deep inspiration breath-hold (DIBH) radiotherapy after lumpectomy were enrolled at Herlev and Gentofte hospital from February 2016 to April 2017 (Table 1). All included

patients gave informed consent to participate in the clinical protocol approved by the Copenhagen Regional Committee on Health Research Ethics (No. H-15010813). One patient left the study before the first treatment fraction (no reason given), while 2 others left after the first 4 treatment fractions (one due to the CBCT procedure and one due to shoulder pain).

Table 1: Summary of included patients.

Patient characteristics	**Total**
No. of patients	40
Fractionation scheme	
- Normofractionated (50 Gy/25 fx, 5 fx per week)	1
- Hypofractionated (40 Gy/15 fx, 5 fx per week)	39
Gating area at xiphoid process	39
Gating area at right breast	1
Mean age [y]	61 [35 to 81]
Gating window width (mean ± 1SD [range]) [mm]	2.7 ± 0.6 [2 to 4]
Gating amplitude (mean ± 1 SD [range]) [mm]	14.6 ± 4.0 [7.9 to 21.8]

SD: standard deviation. Fx: fractions

2.2 Optical surface scans

Before the DIBH planning CT scan, a free breathing (FB) surface scan covering the surface area from approximately the navel to above the head (ROI_{full}) was acquired using an OS-system (Sentinel, C-RAD Positioning AB, Uppsala, Sweden). This surface was used to place the gating area for monitoring the respiratory breathing motion and used as reference for surface based setup [11]. The mean time from surface to CT scan was 9 ± 3 minutes (1 SD) and included DIBH training. The surface scans recorded with the single camera OS-system (Catalyst, C-RAD Positioning AB) in the treatment rooms were averaged over several scans acquired over 5 s to minimize the artifacts caused by respiration motion. This breathing averaging was not available in the CT room.

Retrospectively, two additional surface references were created using parts of the ROI_{full} surface, $ROI_{bothBreast}$ covering both breasts and $ROI_{leftBreast}$ covering only the target breast (Fig. 1). The registration of the treatment surface to the three different reference surfaces was calculated in a test application, provided by the vendor of the OS-system, enabling multiple registrations in a batch file. The registrations to ROI_{full}

were also performed in the clinical OS-software and small differences ($\leq$ 1 mm for 512 out of 537 registrations) were observed compared to the test application. Only the registrations made in the test application were used, but the conclusions of the study would not be affected by this.

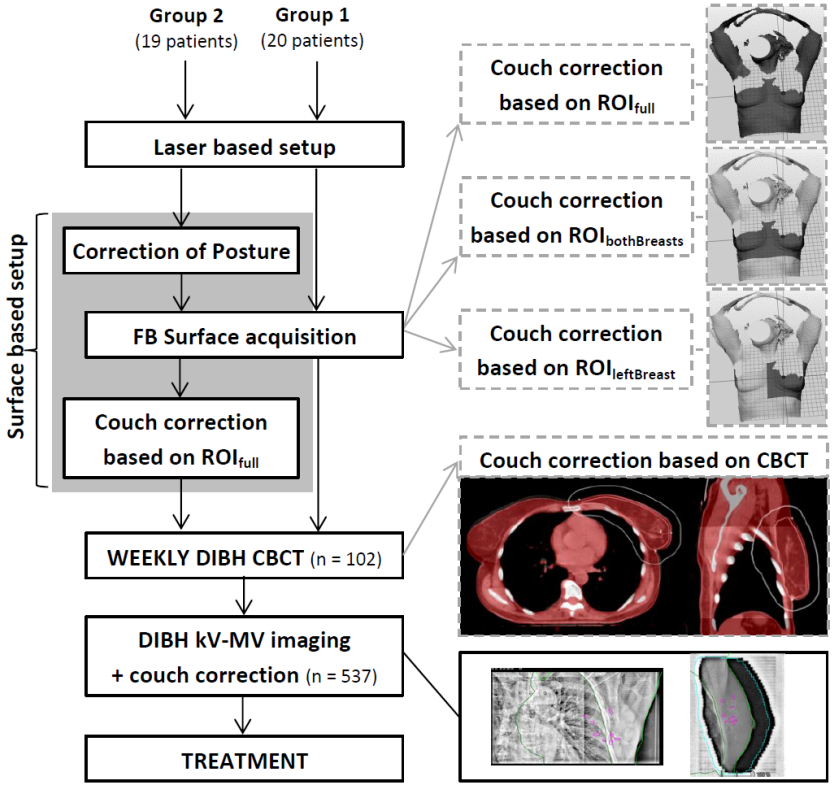

Fig. 1: Schematic outline of the imaging protocol. The protocol used clinically is in solid-line boxes, while the virtual protocol based on CBCT and surface based setup is in grey dash-line boxes. For group 1 the surface based setup did not include arm posture correction. In lower right corner the registration volume of interest (CTV plus a 2 cm margin) used for the automatic soft-tissue registration is presented with white lines on the DIBH CT images. The red coloured voxels within the volume of interest are used for the registration.

2.3 Experimental Design

Patients were alternately assigned to one of two groups (1 or 2) by the radiation therapists prior to radiotherapy (Fig. 1). The patients were placed on a breast board (Posiboard-2, CIVCO, Iowa) and initially setup in FB based on laser. The posture of the

arms and head were corrected for Group 2, using the colour map of the OS-system projected on to the patient. No colour was projected if the distance between a position in the current surface and the reference surface was smaller than 5 mm. It was assumed that head posture correction had minimal effect on internal anatomy and deformation of breast tissue, and the focus was therefore turned to the arm in the current paper. A FB surface was acquired for both groups and the couch position was recorded. Based on the OS-system, a couch shift was performed for group 2. The system uses a non-rigid registration algorithm between the current surface and the reference surface to calculate the couch shift needed to move the patient to the planned isocenter position [12,13]. The influence of the surface structures are weighted in the calculations, such that the surface close to the isocenter has a higher influence. Weekly DIBH CBCTs were acquired (starting from fraction 2), but only used for retrospective analysis. Patient position was verified daily during breath-hold using anterior-posterior kV-images acquired with an On-Board Imager (Varian Medical Systems, CA, USA) and tangential portal field MV-images (kV-MV). The mean time from CBCT to kV-MV acquisition was 5 ± 3 minutes. Registration of the kV-MV images to the digitally reconstructed radiographs were performed online by experienced radiation therapists, using the medial end of the clavicle, the chest wall and the caudal contour of the breast. If setup errors exceeded 1 cm in the vertical direction the patient position was verified after couch correction using a new set of kV-MV images.

For one patient in group 2 a new surface was acquired after kV-MV and used as reference for the remaining fractions, as the posture from the original reference was not realisable over multiple fractions.

2.4 CBCT Registrations

The CBCT images were retrospectively registered to the planning CT using Offline Review 13.6 (Varian Medical Systems, CA, USA) with six degrees of freedom. Initially an automatic match was performed using the Hounsfield units in the range from -150 to 150 to cover the soft tissue and a volume of interest including the clinical target volume (CTV, whole breast) plus an isotropic margin of 2 cm (Fig. 1) [14]. The 2 cm margin was to ensure tissue to air image contrasts for more stable registration. The match was evaluated by one observer (SNB), and if needed manual adjustments were made to get a better match on the area of the chest wall directly posterior to the target area. The sternum, the surgical clips and the papilla mammae were used as additional guidelines.

To improve the registration quality, the registrations that were not straight-forward were identified and refined if possible by a medical physicist with more than 15 years of experience in mamma image registrations. Refinement was ≤ 3 mm and ≤ 1.1° for all registrations, except for one with a roll difference of 3.8°.

2.5 Data processing

A total of 537 treatment fractions with daily setup data based on laser, surface, kV-MV and 102 treatment fractions with weekly CBCT were analysed in MATLAB R2017b (The MathWorks, Inc., Natwick USA). This was after exclusion of 36 fractions due to different technical issues. Each patient had 1-4 CBCT scans; the low number for some patients was due to different technical issues. Group 1 without posture correction included 275 fractions (54 of them with CBCT) while group 2 with posture correction included 262 (48 of them with CBCT).

For each fraction the couch position was extracted after setup based on laser, surface using the three different ROIs (ROI_{full}, $ROI_{bothBreast}$, $ROI_{leftBreasts}$), kV-MV and CBCT when available. In this way the potential treatment positions were known had the setup been based on either one of these six methods. The translation setup errors (lateral, longitudinal and vertical) were then evaluated using CBCT as ground truth and kV-MV as ground truth, and the resulting length of the error vector $|\Delta|$ was calculated. The rotational setup errors (yaw, roll, and pitch) were only evaluated using CBCT as ground truth. The translation setup errors with a length ≤ 4 mm were considered to be within clinical tolerance according to local guidelines, while setup errors with a length > 10 mm were considered gross. The clinical tolerance for $|\Delta|$ was ~7 mm, corresponding to a setup error equal to 4 mm in each direction.

2.6 Statistics

To compare the median of $|\Delta|$ using the different setup methods the Wilcoxon sign rank test was used for paired data (group 1 and 2 combined), while Wilcoxon rank sum test was used for the unpaired data when comparing group 1 and group 2 using a specific setup method. The smallest difference in the median of $|\Delta|$ between group 1 and 2 for kV-MV based setup that could be statistically significantly detected was identified. This was done by element-wise adding an increasing percentage of each $|\Delta|$ to the group with the largest median, until a significant difference could be detected. To test if the mean setup error was significantly different from zero in the different directions student t-test

was performed. To test for difference between percentages the chi-squared test was performed. Significance levels of the different tests were set to $\alpha = 0.05$.

3. Results

In the following the results from the 102 treatment fractions with CBCT scans will be presented. It will be emphasized if the presented results instead are based on the 537 treatments fractions with daily kV-MV imaging; these results will however only be presented if the conclusions differ significantly from the CBCT based conclusions.

The median of the error vector length ($|\Delta|$) from kV-MV based setup was not significantly different for the patients with arm posture correction (4.2 mm) compared to the patients without arm posture correction (4.4 mm) (Table 2). It was found that the difference had to be at least 1.1 mm to be detectable as significant. The median $|\Delta|$ from the surface based setup using ROI_{full} was significantly lower with arm posture correction compared to no correction with kV-MV as the ground truth. However, a significant difference was not detectable for surface based setup when the CBCT was used as ground truth, although pointing in the same direction. The patients assigned to group 2 (with arm posture correction) did not need arm posture correction in 15 % of the fractions as the surface was within tolerance (< 5mm).

Table 2: Statistics for the length of the error vector $|\boldsymbol{\Delta}|$ [mm] with CBCT and kV-MV as ground truth presented with arm posture correction and without arm posture correction (in parenthesis).

	CBCT as ground truth (n = 102)		kV-MV as ground truth (n = 537)	
	Median	95% CI	Median	95% CI
Surface ROI_{full}	5.6 (5.9)	4.8-6.4 (4.9-6.8)	**5.1 (5.7)**	**4.7-5.5 (5.4-6.1)**
Surface $ROI_{bothBreasts}$	6.2 (6.1)	5.3-7.2 (5.1-7.0)	6.1 (5.8)	5.7-6.5 (5.4-6.2)
Surface $ROI_{leftBreast}$	6.3 (6.0)	5.2-7.4 (5.2-6.9)	6.5 (6.0)	6.0-7.0 (5.6-6.4)
Laser	6.9 (6.4)	5.9-7.8 (5.4-7.4)	7.0 (6.9)	6.5-7.5 (6.5-7.4)
kV-MV	4.4 (4.2)	3.7-5.0 (3.7-4.7)	-	-

CI: confidence interval of the median. Bold style indicates the median length of the error vector is significantly different with and without arm posture correction.

The median |Δ| from surface based setup using ROI_{full} was significantly lower compared to setup based on laser and surface using $ROI_{bothBreasts}$ or $ROI_{leftBreast}$ (Table 3). Eighty-seven percent of the |Δ| from kV-MV were ≤ 7 mm. The corresponding percentages for setup based on surface using ROI_{full} and laser were 65 % and 53 %, respectively (Fig. 2). A higher percentage of setup errors with a length ≤ 4 mm were observed in the lateral direction compared to the longitudinal and vertical direction for the different setup methods studied (Table 3). The percentage of gross setup errors (100% -P_{9mm}) was highest in the longitudinal direction for surface based setup regardless of ROI. A gross kV-MV based setup error was only observed in the vertical direction. The gross error was from a patient who was noted to having problems with the DIBH technique by the radiation therapist. Rotational errors for the surface based setup had a mean value around -1° to 1° (Table 4).

Table 3: Statistics for the translational setup errors using surface, laser and kV-MV with CBCT as ground truth (n = 102 registrations).

	μ (1SD) [mm]			Median (95% CI) [mm]	P_4,P_9 [%]			P_7,P_{16} [%]
	Δ_{lat}	Δ_{lng}	Δ_{vrt}	$\|\mathbf{\Delta}\|$	$\|\Delta_{lat}\|$	$\|\Delta_{lng}\|$	$\|\Delta_{vrt}\|$	$\|\mathbf{\Delta}\|$
Surface ROI_{full}	-0.1 (3.0)	-1.9 (4.0)*	0.5 (4.1)	5.8 (5.2-6.4)	88,100	70,95	71,99	65,100
Surface $ROI_{bothBreasts}$	-0.5 (3.1)	-2.3 (4.1)*	0.8 (4.2)	**6.2 (5.5-6.8)**	83,100	70,95	73,99	60,99
Surface $ROI_{leftBreast}$	-0.8 (3.6)*	-2.2 (4.2)*	0.8 (4.2)*	**6.2 (5.6-6.9)**	**78**,99	69,95	72,99	55,99
Laser	1.5 (3.9)*	-0.9 (4.0)*	-1.5 (4.9)*	**6.5 (5.8-7.2)**	**74**,97	78,97	63,96	53,98
kV-MV	-0.4 (2.6)	0.9 (3.0)*	-0.2 (3.4)	**4.2 (3.9-4.6)**	91,100	**85,100**	**84**,99	**87**,99

μ: mean. SD: standard deviation. Δ_{lat}, Δ_{lng}, Δ_{vrt}: The setup error in the lateral, longitudinal and vertical direction, respectively. A negative value corresponds to the treatment position of the evaluated method being more to the right, or more caudally or posteriorly compared to the treatment position based on CBCT. CI: confidence interval. $|\mathbf{\Delta}|$: Length of error vector. P_4 and P_9: the percentage of setup errors with a length ≤ 4 mm and ≤ 9 mm, respectively. P_7 and P_{16}: the percentage of $|\mathbf{\Delta}| \leq$ ~7 mm and ≤~16 mm. *indicates that the mean setup error was significantly different from 0. Bold style indicates that the median of |Δ| or the percentages was significantly different from the results with surface based setup using ROI_{full}. Results with kV-MV as ground truth are included in Supplementary Data.

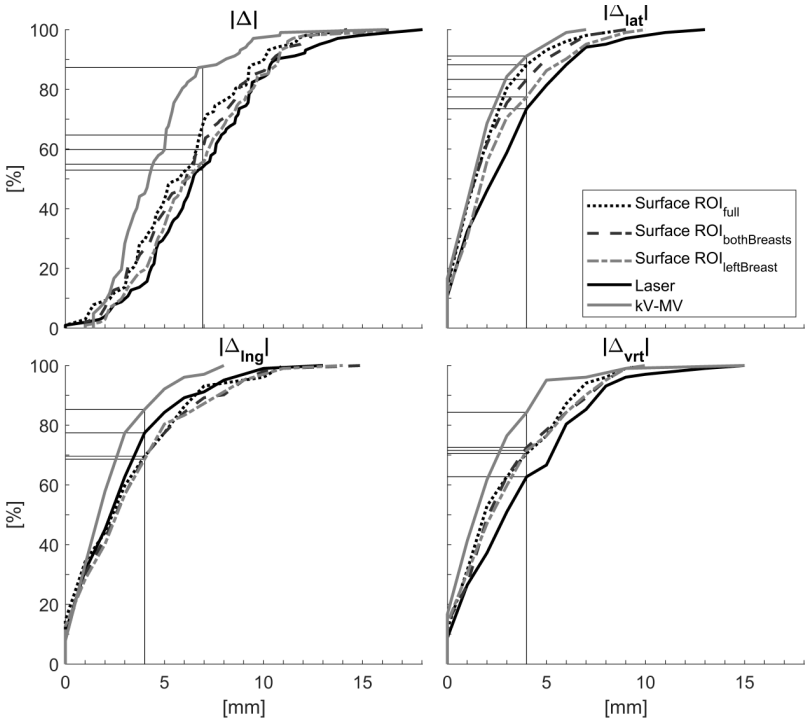

Fig. 2: Cumulative plots using the different setup techniques with CBCT as ground truth (n = 102 registrations). For the length of the error vector $|\boldsymbol{\Delta}|$, the percentages of setup errors with a radius ≤ ~7 mm are marked with a horizontal line. The percentages of setup errors with a length ≤ 4 mm are marked with a horizontal line for the lateral ($|\Delta_{lat}|$), longitudinal ($|\Delta_{lng}|$) and vertical ($|\Delta_{vrt}|$) direction.

Table 4: Statistics for the rotational setup errors using surface and laser with CBCT as ground truth (n = 102 registrations).

	μ (1SD) [°]			$P_{3°}$ [%]		
	Δ_{yaw}	Δ_{roll}	Δ_{pitch}	$\lvert\Delta_{yaw}\rvert$	$\lvert\Delta_{roll}\rvert$	$\lvert\Delta_{pitch}\rvert$
Surface ROI_{full}	0.2 (1.4)	-0.5 (1.6)*	0.9 (1.8)*	94	89	81
Surface $ROI_{bothBreasts}$	0.1 (1.4)	-0.7 (1.5)*	1.2 (1.8)*	94	91	84
Surface $ROI_{leftBreast}$	-0.2 (2.2)	-0.8 (1.8)*	1.0 (1.7)*	86	84	84
Laser	0.3 (1.2)*	0.1 (1.2)	0.2 (1.7)	97	100	90

μ: mean. SD: standard deviation. $P_{3°}$: the percentage of setup errors (ignoring +/-) below or equal to 3°. Δ_{yaw}, Δ_{roll}, Δ_{pitch}: The rotational setup error around the vertical axis, the longitudinal axis and the lateral axis, respectively. * indicates that the mean setup error was significantly different from 0.

4. Discussion

4.1 Arm posture correction vs. no arm posture correction

The primary aim of this study was to investigate if arm posture correction using the OS-system leads to improved kV-MV or surface based setup. No indications of improvement in kV-MV based setup were observed, showing that this setup technique is robust in regard to the arm position variation observed when patients are placed in a breast board. With the current data we would have been able to identify it as significant if the median difference had been at least 1.1 mm. The possible improvement of kV-MV based setup with arm posture correction has to our knowledge not been studied earlier, thus we have no clear data to compare with. However, in the current study it was hypothesised that the kV-MV based setup could be improved by ensuring correct arm posture as this could lead to smaller variation of the lateral clavicle position [9]. That we do not see a significant difference can be that the medial end of the clavicle is not affected much by the arm posture. An alternative explanation is that the registration of the kV-MV images to the digitally reconstructed radiographs was performed using not only the medial end of the clavicle but also the chest wall and caudal contour of the breast, averaging out the effect. Although we did not see an improvement, it is worth emphasizing that the relation between arm posture and the position of the supraclavicular lymph nodes and outline of corpus mammae was not investigated, and may be important. Deformation of the breast tissue can lead to deviations between planned and delivered dose [15].

Arm posture correction lead to a significant improvement of the surface based setup when the arms were included in the surface (ROI_{full}) used for registration. Although the improvement was significant, it was still small, which partly can be explained by the underlying OS-system algorithm for isocenter calculation, where surface far from the isocenter (as the arm) has lower influence than surface close to the isocenter.

4.2 Evaluation of kV-MV, laser and surface based setup (Group 1 and 2 combined)

This study did not suggest that the surface based setup makes kV-MV based setup redundant. This is based on a significantly larger median $|\mathbf{\Delta}|$ from surface based setup (5.8 mm) compared to kV-MV based setup (4.2 mm). In addition there were a

significantly larger percentage of kV-MV based setup errors with a length within the clinical tolerance (≤ 4mm) in the longitudinal and vertical direction, together with a significant smaller percentage of gross setup errors (>10 mm) in the longitudinal direction. The one (and only) gross kV-MV based setup error in the vertical direction was in line with the occasionally large intra-fraction chest wall motion (up to 9.8 mm) from one breath-hold to another that was reported by Lutz et al. [16].The surface based setup errors might have been smaller if a three camera solution had been used instead of the single camera solution [17].

The surface based setup was improved using ROI_{full} compared to $ROI_{BothBreasts}$ and $ROI_{LeftBreast}$. This is in accordance with Pallotta et al. who found reduced setup error when a wider surface was used for the registration and not only the surface in close proximity to the treated region [18]. By using a larger ROI the registration is including more features and the results may be more stable [19]. Stanley et al. have studied surface and laser based setup, but for breast radiotherapy in FB [4]. Our results from the surface based setup are comparable to their results (mean $|\Delta|$ of 6 ± 2 mm). In our study the largest errors were observed in the longitudinal and vertical directions. Similar results has been reported previously and explained to be caused by changes predominately occurring in the longitudinal and vertical directions during respiratory movement [6,20].

No clear improvement was observed with correction of rotational errors using the surface based setup, corresponding to the findings by Alderliesten et al. [21]. The rotational errors could possibly be improved by correcting for systematic errors between CBCT and surface registrations using the registration from the first CBCT.

The surface acquired with the OS-system prior to the planning CT was chosen as reference for the surface based setup, but a reference could have been derived from the planning CT or be acquired with the OS-system during the first treatment day. Previous studies have shown more accurate results using a reference acquired with the OS-system rather than a surface derived from the planning CT [22–24], while other studies show no significant difference [18,25]. The FB surface reference used in this study can give rise to a systematic error due to 1) going from one coordinate system to another (CT to treatment room), 2) the OS-system in the CT room cannot perform breathing averaging [24], 3) patient movement from time of surface to CT acquisition and 4) breath-hold breathing variation from CT to treatment. A significant systematic error was

only observed in the longitudinal direction, which corresponds to the patients sliding down the breast board from time of surface to CT acquisition (on average 9 min. apart), similar has been reported in other studies [25,26].

We tried to use a surface reference from the first treatment day, but the results were not improved significantly (data included in Supplementary Data). The systematic error in the longitudinal direction was eliminated, but a systematic error was introduced in the vertical direction. This can be explained by a baseline shift occurring in the vertical direction during all fractions except from fraction one, as reported by Jensen et al. [27]. A solution to correct for systematic errors is to use an offline strategy ,e.g. no action level protocol [28], in conjunction with surface based setup.

Conclusion

There were no indications for improved kV-MV based setup with arm posture correction. However, arm posture was incorrect in a majority of the fractions, suggesting that the medial position of the clavicle, used to guide the kV-MV based setup, is insensitive to the posture of the arm. Patient setup was significantly improved if based on surface rather than laser suggesting that it can be used as an alternative for initial setup. Regardless, a significant percentage of gross surface based setup errors were observed in the longitudinal direction, stressing that ensuring target position with for example kV-MV is not dispensable.

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6. Conflict of Interest Statement

The research was partly sponsored by C-RAD AB, Uppsala, Sweden. The authors alone are responsible for the content and writing.

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Supplementary data

Other imaging modalities

Weekly Cone-beam CT (CBCT), and kV-MV images were acquired before treatment delivery. All images were acquired during breath-hold using Varian Clinac iX 2300 linear accelerators equipped with an On-Board Imager (OBI) and an electronic portal imaging device (EPID). The number of breath-holds required to perform a complete CBCT scan was 1-6 with a median of 2. The Varian low-dose thorax CBCT protocol was used, and the resolution of the reconstructed CBCT was 1 x 1 x 2 mm^3 in the lateral, vertical and longitudinal direction, respectively.

Treatment surface reference

The results from the surface based setup using a surface reference from the treatment room is presented in Figure 1, Table 1-3. Before being used as reference the surface was corrected according to the couch shift from the kV-MV based setup.

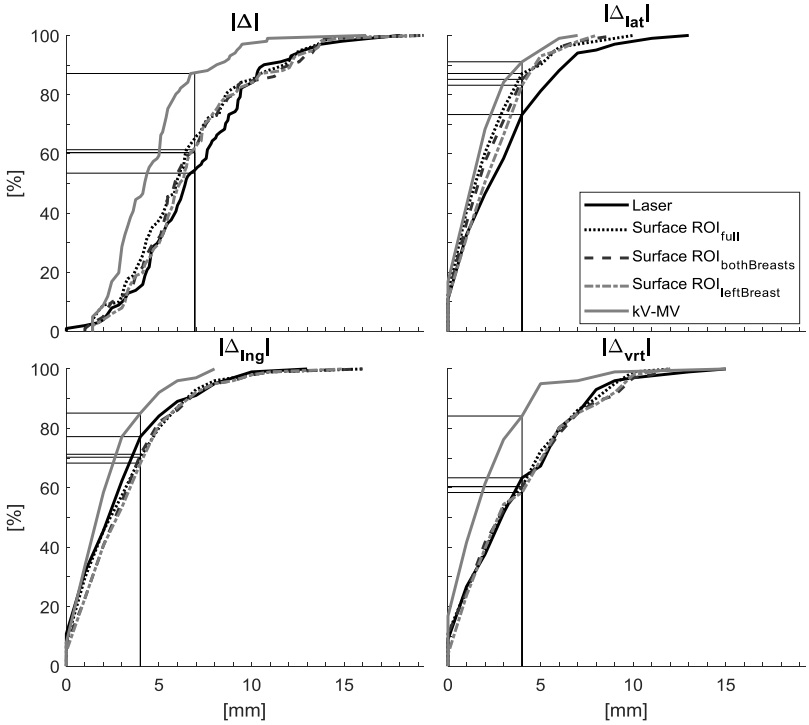

Figure 1: Cumulative plots using the different setup techniques with CBCT as ground. For the length of the error vector $|\Delta|$, the percentages of setup errors with a radius $\leq \sim 7$ mm are marked with a horizontal line. For each translational direction (lateral, longitudinal and vertical) the percentages of setup errors with a length ≤ 4 mm are marked with a horizontal line. A surface from the first fraction was used as reference for all patients, except for two patients where a surface from the second fractions was used due to poor surface quality at the first fraction as the camera settings had not been adjusted properly.

Table 1: Statistics for the length of the error vector |Δ| [mm] with CBCT and kV-MV as ground truth presented with arm posture correction and without arm posture correction (in parenthesis).

	CBCT as ground truth (n = 101)		kV-MV as ground truth (n = 498)	
	Median	95% CI	Median	95% CI
Surface ROI_{full}	5.5(6.2)	4.7-6.3(5.2-7.1)	5.4(5.4)	5.0-5.7(5.0-5.8)
Surface $ROI_{bothBreasts}$	5.5(6.3)	4.8-6.2 (5.4-7.2)	5.5(5.7)	5.2-5.8(5.3-6.1)
Surface $ROI_{leftBreast}$	5.8(6.6)	5.1-6.5(5.9-7.3)	5.8(6.0)	5.4-6.1(5.6-6.5)

CI: confidence interval of the median. No significant difference between the median was detected with or without posture correction.

Table 2: Statistics for the translational setup errors using surface, laser and kV-MV with CBCT as ground truth. A surface scan from first or second treatment fraction was used as reference.

	μ (1SD) [mm]			Median (95% CI) [mm]	P_4,P_9 [%]			P_7,P_{16} [%]
	Δ_{lat}	Δ_{lng}	Δ_{vrt}	$\|\mathbf{\Delta}\|$	$\|\Delta_{lat}\|$	$\|\Delta_{lng}\|$	$\|\Delta_{vrt}\|$	$\|\mathbf{\Delta}\|$
Surface ROI_{full}	0.2 (3.2)	0.4 (4.4)	1.7 (4.6)*	6.0 (5.3-6.7)	87,99	70,97	60,95	61,99
Surface $ROI_{bothBreasts}$	0.0 (3.2)	-0.1 (4.5)	1.8 (4.8)*	5.9 (5.3-6.5)	85,100	71,96	60,91	60,99
Surface $ROI_{leftBreast}$	0.1 (3.3)	0.1 (4.5)	1.9 (4.8)*	6.2 (5.6-6.7)	83,100	68,96	58,92	60,99

μ: mean. SD: standard deviation. Δ_{lat}, Δ_{lng}, Δ_{vrt}: The setup error in the lateral, longitudinal and vertical direction, respectively. CI: confidence interval. $|\mathbf{\Delta}|$: Length of error vector. P_4 and P_9: the percentage of setup errors with a length ≤ 4 mm and ≤ 9 mm, respectively. P_7 and P_{16}: the percentage of $|\mathbf{\Delta}|$ ≤ ~7 mm and ≤~16 mm. *indicates that the mean setup error was significantly different from 0. No significant difference was observed for the median of |Δ| or the percentages from the results with surface based setup using ROI_{full}.

Table 3: Statistics for the rotational setup errors using surface and laser with CBCT as ground truth. The surface scan from first or second treatment fraction was used as reference.

	μ (1SD) [°]			$P_{3°}$ [%]		
	Δ_{yaw}	Δ_{roll}	Δ_{pitch}	$\lvert\Delta_{yaw}\rvert$	$\lvert\Delta_{roll}\rvert$	$\lvert\Delta_{pitch}\rvert$
Surface ROI_{full}	0.2 ± 1.5	-0.5 ± 1.5*	0.7 ± 1.8*	93	94	87
Surface $ROI_{bothBreasts}$	-0.1 ± 1.6	-0.6 ± 1.5*	0.8 ± 1.9*	91	92	82
Surface $ROI_{leftBreast}$	-0.4 ± 2.1	-0.7 ± 1.7*	0.9 ± 2.0*	86	89	82

Δ_{yaw}, Δ_{roll}, Δ_{pitch}: The rotational setup error around the vertical axis, the longitudinal axis and the lateral axis, respectively. $P_{3°}$: the percentage of setup errors (ignoring +/-) below or equal to 3°. * indicates that the mean setup error was significantly different from 0.

Results for the 537 kV-MV treatment fractions

Pre-CT surface reference

The setup errors from the 537 treatment fractions with setup based on surface and laser using kV-MV as ground truth is presented in Figure 2 and Table 4.

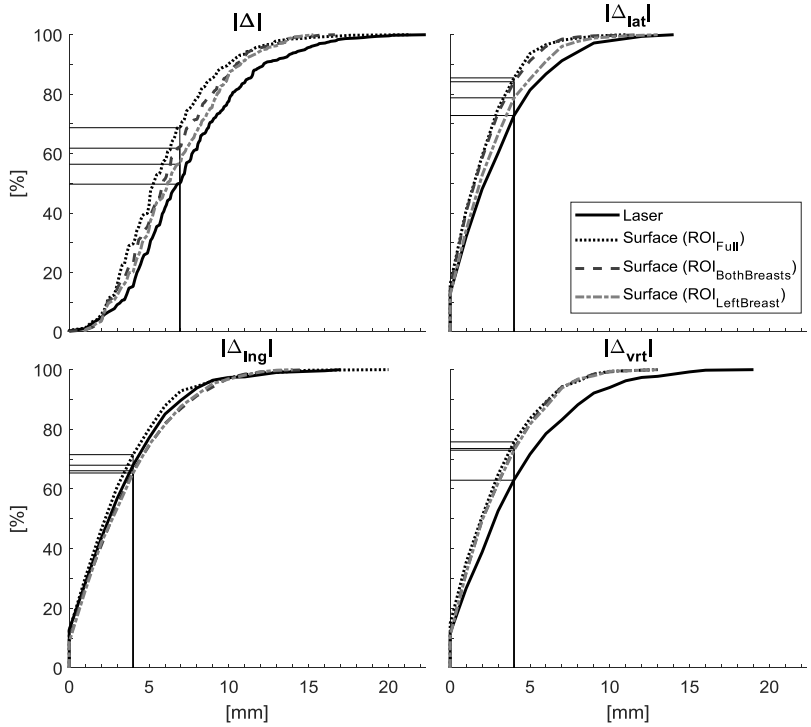

Figure 2: Cumulative plots using the different setup techniques with kV-MV as ground. For the length of the error vector |Δ|, the percentages of setup errors with a radius ≤ ~7 mm are marked with a horizontal line. For each translational direction the percentages of setup errors with a length ≤ 4 mm are marked with a horizontal line. One vertical error of 33 mm using laser based setup has been left out of the plot.

Table 4: Statistics for the translational setup errors using surface, laser with kV-MV as ground truth.

	μ (1SD) [mm]			Median (95% CI) [mm]	P_4,P_9 [%]			P_7,P_{16} [%]
	Δ_{lat}	Δ_{lng}	Δ_{vrt}	$\|\boldsymbol{\Delta}\|$	$\|\Delta_{lat}\|$	$\|\Delta_{lng}\|$	$\|\Delta_{vrt}\|$	$\|\boldsymbol{\Delta}\|$
Surface ROI_{full}	0.2 (3.1)	-1.9 (4.0)*	0.6 (3.9)*	5.4 (5.1-5.6)	86,99	72,96	76,99	69,99
Surface $ROI_{bothBreasts}$	-0.2 (3.2)	-2.4 (4.2)*	0.8 (3.9)*	**5.9 (5.6-6.2)**	84,100	66,94	74,99	**62**,100
Surface $ROI_{leftBreast}$	-0.8 (3.6)*	-2.4 (4.2)*	0.8 (4.0)*	**6.2 (5.9-6.5)**	**79**,99	**65**,95	73,98	**56,100**
Laser	1.4 (4.1)*	-1.3 (4.5)*	-1.1 (5.5)*	**7.0 (6.7-7.3)**	**73,97**	68,97	**63,92**	**50,97**

μ: mean. SD: standard deviation. Δ_{lat}, Δ_{lng}, Δ_{vrt}: The setup error in the lateral, longitudinal and vertical direction, respectively. CI: confidence interval. $|\boldsymbol{\Delta}|$: Length of error vector. P_4 and P_9: the percentage of setup errors with a length ≤ 4 mm and ≤ 9 mm, respectively. P_7 and P_{16}: the percentage of $|\boldsymbol{\Delta}| \leq$ ~7 mm and ≤~16 mm. *indicates that the mean setup error was significantly different from 0. *indicates that the mean setup error was significantly different from 0. Bold style indicates that the median of $|\Delta|$ or the percentages was significantly different from the results with surface based setup using ROI_{full}.

Treatment surface reference

The results from the surface based setup using a surface from the treatment room are presented Figure 3 Table 5. Before being used as reference the surface was corrected according to the couch shift from the kV-MV based setup. Due to this correction, one fraction was left out of the analysis for each patient. This left 498 out of the 537 fractions for the 39 included patients.

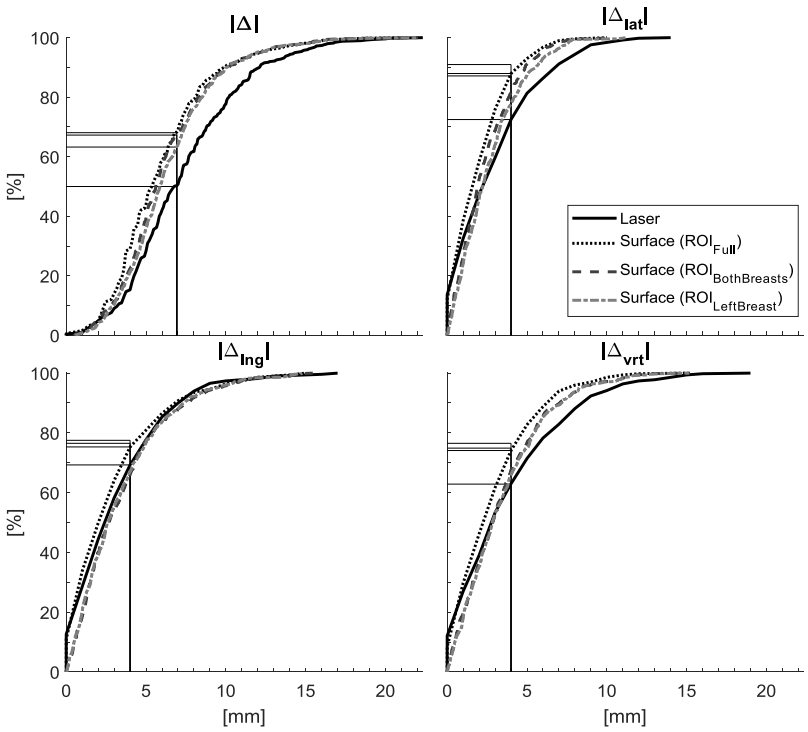

Figure 3: Cumulative plots using the different setup techniques with kV-MV as ground (n = 498 registrations). For the length of the error vector |Δ|, the percentages of setup errors with a radius ≤~7 mm are marked with a horizontal line. For each translational direction the percentages of setup errors with a length ≤4 mm are marked with a horizontal line. A surface from the first fraction was used as reference for all patients, except for two patients where a surface from the second fractions was used due to poor surface quality at the first fraction as the camera settings had not been adjusted properly. One vertical error of 33 mm using laser based setup has been left out of the plot.

Table 5: Statistics for the translational setup errors using surface and laser with kV-MV as ground truth (n = 498 registrations). A surface scan from first or second treatment fraction was used as reference.

	μ (1SD) [mm]			Median (95% CI) [mm]	P_4,P_9 [%]			P_7,P_{16} [%]
	Δ_{lat}	Δ_{lng}	Δ_{vrt}	$\|\boldsymbol{\Delta}\|$	$\|\Delta_{lat}\|$	$\|\Delta_{lng}\|$	$\|\Delta_{vrt}\|$	$\|\boldsymbol{\Delta}\|$
Surface ROI_{full}	0.1 (3.0)	0.4 (4.4)*	1.7 (3.7)*	5.4 (5.1-5.6)	88,100	75,95	74,97	68,98
Surface $ROI_{bothBreasts}$	0.1 (3.0)	-0.2 (4.5)	1.8 (3.9)*	**5.6 (5.4-5.9)**	91,100	78,96	77,97	67,99
Surface $ROI_{leftBreast}$	0.2 (3.3)	0.1 (4.5)	1.8 (3.9)*	**5.9 (5.6-6.1)**	87,99	77,96	75,97	63,99

μ: mean. SD: standard deviation. Δ_{lat}, Δ_{lng}, Δ_{vrt}: The setup error in the lateral, longitudinal and vertical direction, respectively. CI: confidence interval. $|\boldsymbol{\Delta}|$: Length of error vector. P_4 and P_9: the percentage of setup errors with a length ≤ 4 mm and ≤ 9 mm, respectively. P_7 and P_{16}: the percentage of $|\boldsymbol{\Delta}|$ ≤ ~7 mm and ≤~16 mm. *indicates that the mean setup error was significantly different from 0. Bold style indicates that the median of $|\Delta|$ or the percentages was significantly different from the results with surface based setup using ROI_{full}.

PAPER II

Optical Surface Scanning for Respiratory Motion Monitoring in Radiotherapy: a Feasibility Study

Optical surface scanning for respiratory motion monitoring in radiotherapy: a feasibility study

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ABSTRACT

Purpose. We evaluated the feasibility of a surface scanning system (Catalyst) for respiratory motion monitoring of breast cancer patients treated with radiotherapy in deep inspiration breath-hold (DIBH). DIBH is used to reduce the radiation dose to the heart and lung. In contrast to RPM, a competing marker-based system, Catalyst does not require an object-marker on the patient's skin.

Materials & Methods. Experiment 1: a manikin was used to simulate sinusoidal breathing. The amplitude, period and baseline (signal value at end-expiration) were estimated with RPM and Catalyst. Experiment 2 and 3: the Quasar phantom was used to study if the angle of the monitored surface affects the amplitude of the recorded signal.

Results. Experiment 1: we observed comparable period estimates for both systems. The amplitudes were 8 ± 0.1 mm (Catalyst) and 4.9 ± 0.1 mm (RPM). Independent check with in-room lasers showed an amplitude of approximately 8 mm, supporting Catalyst measurements. Large baseline errors were seen with RPM. Experiment 2: RPM underestimated the amplitude if the object-marker was angled during vertical motion. This result explains the amplitude underestimation by RPM seen in Experiment 1. Experiment 3: an increased (fixed) surface angle during breathing motion resulted in an overestimated amplitude with RPM, while the amplitude estimated by Catalyst was unaffected.

Conclusion. Our study showed that Catalyst can be used as a better alternative to the RPM. With Catalyst, the amplitude estimates are more accurate and do not depend on the angle of the tracked surface, and the baseline errors are smaller.

Keywords: Optical surface scanning, respiratory motion compensation, gating, deep inspiration breath-hold, breast cancer, radiotherapy, motion management, RPM.

1. INTRODUCTION

Radiotherapy is used as adjuvant treatment of breast cancer to reduce the risk of both local cancer recurrence and breast cancer death [1]. In left-sided breast cancer, the use of radiotherapy has induced an increased risk of cardiac mortality [2]. The rate of ischemic heart disease has been found to be proportional to the mean dose to the heart [3].

Much effort has been done to reduce the radiation dose to the heart, for example optimization of the dose plans. One other method is a motion management technique called deep inspiration breath-hold (DIBH). Here it is utilized that the distance between target (breast and lymph nodes) and heart is increased when the lungs are inflated. Several studies have shown that irradiation during DIBH leads to significantly reduced dose to the heart compared to irradiation during free breathing [4][5][6]. Studies have also shown that visual guidance for the patient can increase the stability of the breath hold throughout treatment [7][8]. Visual guidance requires monitoring of the respiration motion.

Conventional methods for motion monitoring the respiration motion of breast cancer patients include tracking of physical markers placed on the patient's skin close to the target area. One marker-based system widely used is the Real-time Position Management (RPM) system (Varian Medical Systems, Palo Alto, CA) [9]. One of the drawbacks of RPM is its sensitivity to the angle of the surface, i.e. tilting of the object-marker during breathing motion. Tilting introduces errors in the measured surface motion signal [10].

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A new method tracks the patient's surface directly, and enables acquisition of surface data within a selected area (detection area) in real-time. Such surface scanning systems are commercially available with the systems GateCT/GateRT (VisionRT, London, UK) and Catalyst/Sentinel (Catalyst, C-rad Positioning AB, Uppsala, Sweden). Compared to marker-based systems, the surface scanning systems do not require an object-marker on the patient's skin and with Catalyst/Sentinel it is possible to track the motion using two different spatial areas simultaneously.

At our radiotherapy unit at Herlev Hospital, University of Copenhagen, we are currently replacing our method for motion monitoring from RPM to Catalyst. This study encompasses parts of the validation tests performed prior to the implementation. In the present study we compared Catalyst with RPM in regard to estimating the amplitude (half peak-to-peak value), period and baseline (signal value at end-expiration) of the surface motion signal (Experiment 1). We also studied if the surface angle affected the measured signal of the surface motion using both systems (Experiment 3) and RPM only (Experiment 2).

2. MATERIALS & METHODS

Experiment 1 and 3 were done with Catalyst and RPM (with two-dot object-marker), while Experiment 2 was done with RPM only. Catalyst consists of a projector, which projects a sequence of patterns onto the surface of the patient, and a camera recording the patterns. From the recorded images the motion signal from a selected area (detection area) on the skin can be extracted. RPM consists of an infra-red camera and an object-marker, which is placed on the surface that is tracked. The Catalyst and RPM camera were both mounted in the ceiling of the treatment room.

In Experiment 1, a phantom based on a CPR manikin (Little Anne, Laerdal Medical, Stavanger, Norway) was used to simulate sinusoidal breathing motion. In Experiment 2 and 3 measurements were done with a commercially available respiratory motion phantom (Quasar, Modus Medical Devices Inc., London, Canada), which can simulate sinusoidal breathing motion.

2.1 Experiment 1: Shape and baseline of the motion signal

In this experiment we used the CPR manikin to compare Catalyst with RPM in regard to estimating the amplitude, period and baseline of the surface motion signal, Figure 1. Measurements were done with the manikin's head centred at the reference point (isocenter) and with the manikin displaced laterally, longitudinally and vertically, Figure 1. Each measurement lasted 45 s. The object-marker from RPM was placed at a fixed location with one corner at xiphoideus and approximately 2 cm below the right breast on the manikin. The Catalyst detection area was set at the corresponding location on the left side of the manikin.

From the surface motion signals measured with RPM and Catalyst the amplitude (half peak-to-peak value), period and baseline (signal value at end-expiration) were estimated for each position of the manikin, Figure 2. The amplitude (A) and period (T) were estimated by fitting the measured signal y(t) using

$$y(t) = A \cdot sin\left(\frac{2\pi}{T} \cdot t\right) \quad (1)$$

To detect baseline errors, the baseline of the motion signal was estimated at each manikin position relative to the baseline with manikin position at isocenter. The amplitude of the surface motion was visually validated using the in-room lasers and a millimetre scale plastered on the side of the object-marker.

2.2 Experiment 2: Tilting of the object-marker during vertical movement

In this experiment we performed measurements with RPM using vertical movement of the object-marker with and without tilting of the object-marker, Figure 3A.This was done with the object-marker positioned with an angle of 0, 8, 16 or 23°, followed by 10 mm vertical (upward) movement, using the Quasar phantom. The angle was then kept constant or changed according to Figure 4. The motion signal was measured for at least 15 s at each position, with a sampling frequency of 25 Hz.

The design of the manikin used in Experiment 1 causes changes in the surface angle and thus tilting of the object-marker, Figure 5. Setup B in Figure 4 simulates the situation with the tilting of the object-marker on the surface of the manikin during breathing from Experiment 1. Setup C simulates a situation where the object-marker is tilted with the same angle during the whole breathing motion.

It should be noted that the results in Experiment 2 have been adjusted by a factor of 0.5. This has been done in order to be able to compare the results with Experiment 1 and 3, where the amplitude is giving by half the peak-to-peak value.

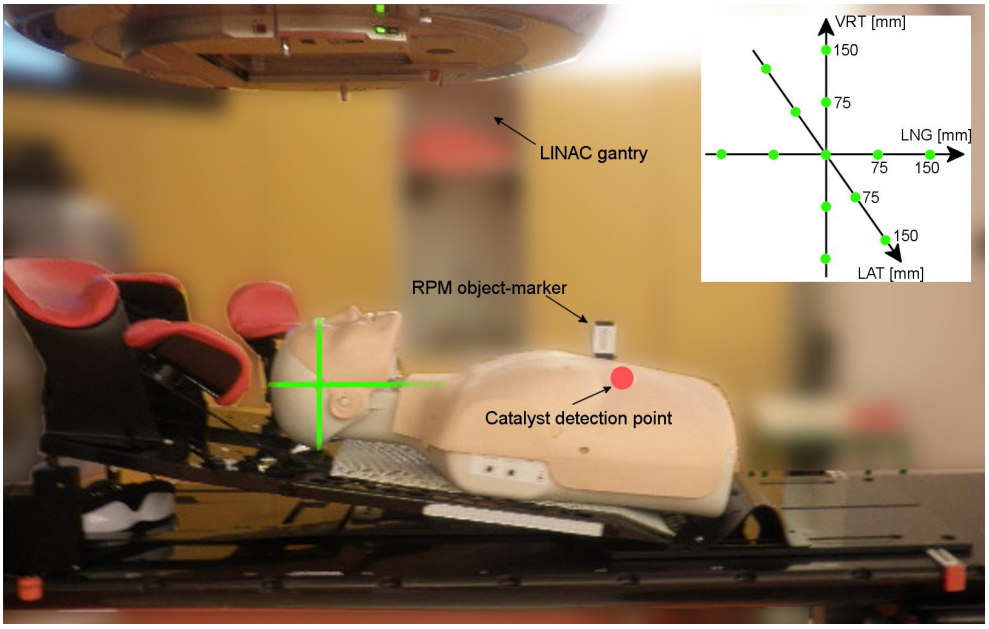

Figure 1: Experiment 1: the manikin placed on the breast board (Posiboard-2, CIVCO, Kalona, Iowa) in the treatment room below the gantry of the linear accelerator (LINAC). Measurements were done with the manikin's head placed at different positions, which are showed with green dots in the coordinate system: i.e. at isocenter (0,0,0) and with lateral (LAT), longitudinal (LNG) and vertical (VRT) manikin displacement of ±75 and ±150 mm. Measurements were done twice at each manikin position, while four measurements were done with the manikin's head centred in the isocenter (two initial, and two final measurements). Before beginning the measurements it was ensured that the object-marker was at a zero degree angle at end-expiration.

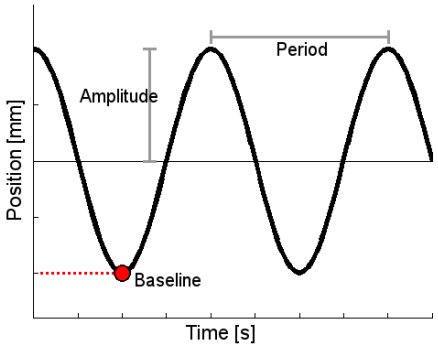

Figure 2: Illustration of the parameters extracted from the surface motion signal: The amplitude (half peak-to-peak value), period and baseline (end-expiration value).

2.3 Experiment 3: Sinusoidal breathing motion with varied angle of the surface

In this experiment we performed measurements using a surface moving in a sinusoidal pattern with both RPM and Catalyst; the surface was angled at 0°, 8° and 16°, Figure 3B. With this setup we tested whether the measured surface motion signal has any surface angle dependency. This experiment is therefore done as a supplement, in order to test whether the results in Experiment 2 is also valid for measurements with a continuously moving surface.

The sinusoidal surface motion signal was generated by Quasar, and had an amplitude of 5 mm (the largest vertical amplitude motion possible with the Quasar phantom) and a period of 4 s. For women, the average breathing amplitude (half peak-to-peak value) at deep inspiration is around 8 mm and the period during free breathing is 4 s [11]. A cardboard was attached to the phantom's movable platform, and the object marker was positioned on top, Figure 3B. The angle of the surface was measured with an application (FreeSpirit – Spirit Level) for iPhone 4S. The angle measurements with the application were verified to be correct within ±1° by a digital angle measurement tool (Husky 9 in. digital lever, Atlanta, Georgia, U.S.). The surface motion signal was measured for at least 50 full periods, measurements were repeated for each surface angle (0°, 8° and 16°).

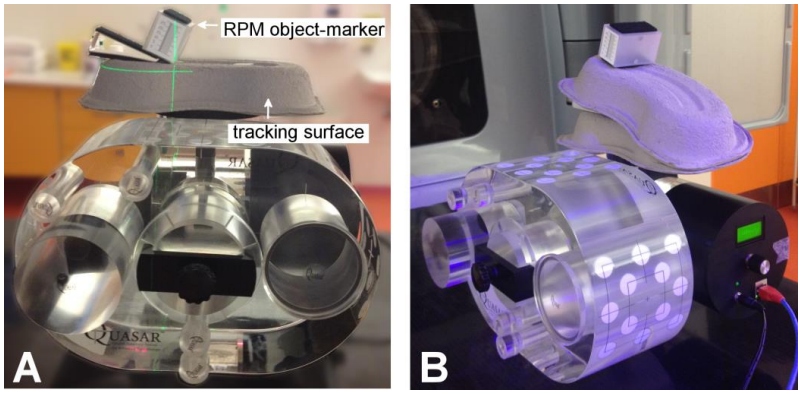

Figure 3: In Experiment 2 and 3 the Quasar phantom was used with modifications to allow for surface tracking with Catalyst and RPM. (A) The setup for Experiment 2: the object-marker tilts during vertical movement (simulation of Experiment 1). (B) The setup for Experiment 3: the surface, and hence the object-marker, is angled during breathing motion.

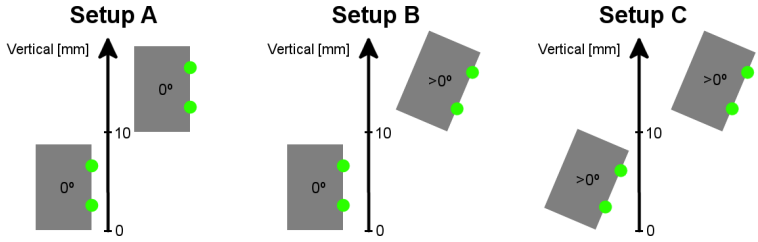

Figure 4: Experiment 2: the 3 setups for measurements. The RPM object-marker (grey rectangle) with the two reflective dots (two green circles), which are tracked by the RPM camera. In Setup A the object-marker is placed in a flat area (0°), and then the object-marker is moved 10 mm upwards and the angle is kept at 0°. In setup B the object-marker is tilted from 0 to 8, 16 or 23° after the 10 mm upward movement. In setup C the object-marker is tilted 8, 16 or 23° throughout the whole measurement.

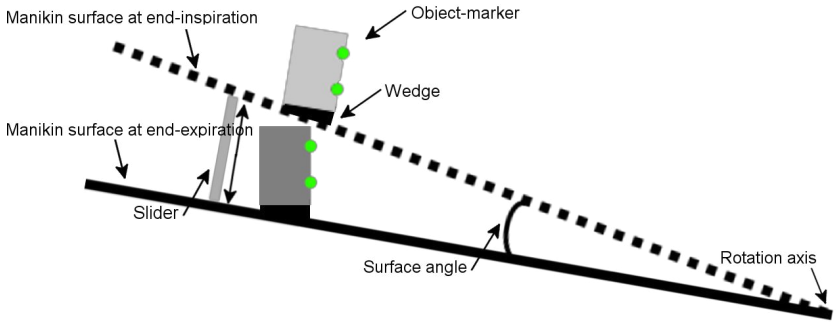

Figure 5: Visualization of how the surface changes during breathing with the manikin (placed on the breast board) used in Experiment 1. The surface is attached at the bottom of the manikin's abdomen (rotation axis) and a slider, placed in the centre of the manikin's thorax region, generates the surface motion. The surface and hence the object-marker will tilt during breathing motion, as a consequence of the design. The wedge below the object-marker ensures that the object-marker is at a zero degree angle at end-expiration. The surface angle changes approximately 8° during breathing motion.

3. RESULTS

3.1 Experiment 1: Shape and baseline of the motion signal

For all manikin positions, the period was estimated to 6.3 ± 0.0 s (mean (μ) ± standard deviation (σ)) for both systems; i.e. there is no significant difference between the period estimated with RPM and Catalyst. The amplitude for all manikin positions was estimated to 8.1 ± 0.1 mm and 4.9 ± 0.1 mm for Catalyst and RPM, respectively. Visual validation with in-room lasers estimated the amplitude to be approximately 8 mm. The amplitude error by RPM is suspected to be introduced by tilting of the object-marker during breathing, Figure 5. The amplitude was seen to be independent of manikin position.

The baseline value for RPM varied with manikin position, Figure 6. For all manikin positions, the largest baseline error was 39.4 mm for RPM and 0.7 mm for Catalyst, Figure 6.

3.2 Experiment 2: Tilting of the object-marker during vertical movement

When moving the surface vertical from one position with the object-marker at 0° to a tiled position, RPM underestimates the amplitude, Setup B in Figure 7. On the contrary, the amplitude is overestimated if the angle of the object-marker is larger than 0° at both vertical positions, Setup C in Figure 7.

3.3 Experiment 3: Sinusoidal breathing motion with varied angle of the surface

There is a tendency to overestimation of the amplitude with the RPM with increasing angle of the object-marker, see Experiment 3 in Figure 7. This supports the results found in Experiment 2 (Setup C). Catalyst gives stable results, which are angle independent.

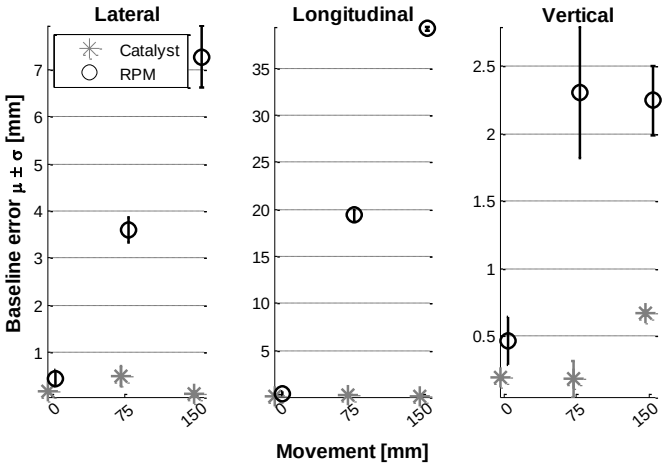

Figure 6: Experiment 1: the mean (μ) and standard deviation (σ) of the baseline error: defined as the absolute difference between (1) the baseline found at the different manikin positions and (2) the baseline found with manikin at isocenter. At 0 mm is the baseline error between (1) the baseline found at the two last measurements at isocenter and (2) the two initial measurements at isocenter.

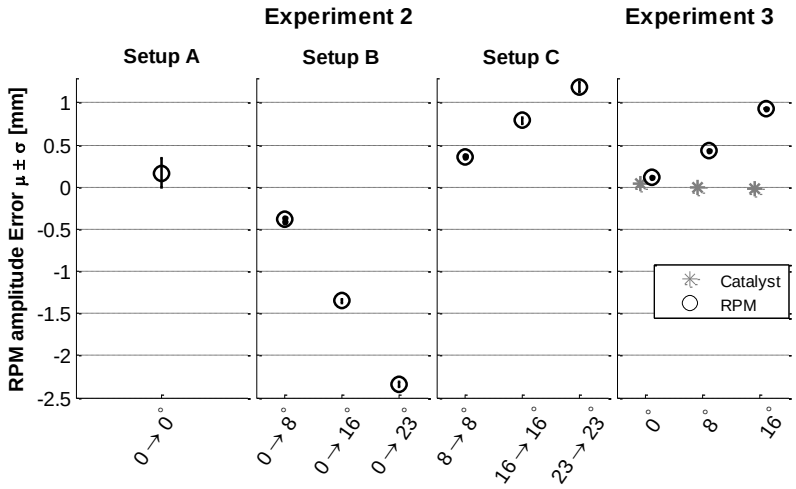

Figure 7: Experiment 2: μ and σ of the amplitude error with RPM. A positive μ corresponds to an overestimation of the measured amplitude. N.B. the results have been adjusted by a factor of 0.5, see paragraph 2.2. Experiment 3: the μ and σ of the amplitude error for Catalyst and RPM for different surface angles.

4. DISCUSSION

We have shown that the RPM and Catalyst acquire signals that yield similar period estimates, while the RPM can have an amplitude error. It was assumed that the amplitude error was caused by tilting of the object-marker during breathing motion, which was supported by a second experiment. We have shown that the amplitude of the surface motion can be both underestimated and overestimated with RPM. This depends on whether the tilt of the object-marker is constant

during the breathing motion (overestimation), or if the tilt of the object-marker changes (from 0 ° initial tilt) during the breathing motion (underestimation).

With Experiment 1 we saw an amplitude error of -3.1 mm with RPM. Part of this error (0.4 mm) can be explained by the 8° tilting of the object-marker according to Experiment 2. The complex structure of the manikin makes it difficult to place the RPM object-marker and the Catalyst detection area in comparable positions, and this may lead to an added uncertainty in the recorded surface motion. A lower amplitude of the surface motion will be generated if the RPM object marker is placed closer to the bottom of the manikin's abdomen (rotation axis) compared to the Catalyst detection area. In addition the object-marker will also move towards the infra-red camera as the surface angle increases. This will, based on Experiment 1 (data is not shown), give rise to a baseline shift that will result in a lower amplitude with RPM.

One of the important prerequisites in radiotherapy is the reproducibility of the patient setup throughout the course of the treatment: from the CT scan for treatment planning, to the delivery of the radiotherapy in the treatment room over several days. Thus it is important that the surface motion signal is reproducible during the entire course of treatment, in order to deliver the planned radiation dose to the target, and meet the dose constraints of the heart. This can partly be ensured by using the same motion tracking system at the CT and treatment room. Reproducible motion tracking can be achieved with both RPM and Catalyst. But for RPM this requires that that any possible tilting of the object-marker is reproduced throughout the treatment course. According to the system reference guide for RPM, 20-25° tilting of the object-marker can give inaccurate amplitude estimates[10]. This statement is valid for both the two-dot object-marker, which we used in this study, and the newer six-dot object maker. In this study we did see amplitude errors of approximately 1 mm with a tilting of only 16°. We have not looked at the six-dot object-marker in the present study.

In contrast to the results for Catalyst, large baseline errors were observed for RPM when the manikin was moved to different positions. In the clinical setting lateral movement of about 75 mm can be necessary if setup imaging with cone beam CT are needed prior to treatment. The baseline error with RPM can be corrected for by acquiring a new baseline by re-tracking the motion signal. If the baseline is not correct the visual guidance of the patient will be incorrect, and the patient will perform a DIBH that is either too deep or to shallow. This can result in incorrect dose delivery such as incomplete target coverage but also increased dose the heart.

RPM showed a surface angle dependency, which can give rise to both amplitude estimates which were too low or too high. We have not investigated to what extend the object-marker tilts in the clinical setting. However, best procedure is to place the object-marker on a flat and stable location on the patient if the measured surface motion is to be accurate. We assume that it is not possible to completely avoid tilting of the object-marker in the clinic, since the patient's surface is not flat and stable during breathing.

5. CONCLUSION

Catalyst can be used as a better alternative to the RPM for DIBH in radiotherapy. Catalyst avoids object-markers on the patient and thus eliminates the effect of the surface angle on the measured motion amplitude. With Catalyst we therefore believe that the reproducibility of the DIBH is improved, and hence that the dose constraints to the heart may be complied better and the target coverage may be better.

Catalyst and RPM have estimates of the amplitude and the period of the measured surface motion signal, which is not affected by any couch movement. However, variation of the surface angle induced both too low and too high amplitude estimates with RPM, while Catalyst was unaffected. This emphasizes the importance of using the same motion management system throughout the course of the treatment (from the CT scan to the treatment room), in order to avoid any errors with the DIBH.

Couch movement during monitoring lead to large baseline errors with RPM, which were not seen with Catalyst. With RPM, couch movement during a treatment session should therefore always be followed by re-tracking, i.e. by acquiring a new baseline to ensure accurate dose delivery. This correction is not necessary with Catalyst.

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PAPER III

Non Interchangeability of Gating Areas Using Surface Scanning in Deep Inspiration Breath-Hold Radiotherapy

The following manuscript is to be submitted as a technical note for Acta Oncologia. The last enclosed draft was edited by me (SNB).

Non-interchangeability of gating areas using surface scanning in deep inspiration breath-hold radiotherapy

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Abstract

Introduction: Deep inspiration breath-hold (DIBH) is used for heart and lung sparing in radiotherapy of breast cancer patients. In this study the feasibility of moving the gating area in-between treatment fractions from the area at the xiphoid process or the right breast to the target (left) breast was investigated. Inter-fraction baseline variation dependency with patient obesity measure (body index) was also investigated.

Material and Methods: The study included 262 left-sided breast cancer patients treated with DIBH radiotherapy after mastectomy (n=52) or lumpectomy (n=210). An optical surface scanning system was used to measure the respiratory motion signal at the gating area at the xiphoid process or right breast. For lumpectomy patients the respiratory motion at the target breast was measured simultaneously with the motion at the gating area. The breath-hold reproducibility was defined as the maximum differences between different breath-hold levels occurring within the same fraction (intra-fraction) or from one fraction to another during the treatment course (inter-fraction). The breath-hold stability was defined as the standard deviation of the difference between respiratory motion signal at the gating area and area above the target breast.

Results: An acceptable inter- and intra-fraction reproducibility (≤5 mm) of the breath-holds at the target breast was seen in 44% and 82% of the patients, respectively. The mean stability of all breath-holds was below 2 mm. The standard deviation of the respiratory motion baseline increased significantly with patient body index, and was higher for mastectomy patients than lumpectomy patients.

Conclusion: The inter-fraction reproducibility was poor for the majority of patients, which implies that the gating area in general should not be moved from the xiphoid process or the right breast to the target breast during the treatment course. Obese patients (with high body index) showed larger inter-fraction baseline variation, indicating larger setup errors for these patients.

Keywords: Deep inspiration breath-hold, gating, breast cancer, optical surface scanning, radiotherapy.

1. Introduction

Breast cancer patients often receive radiotherapy as part of their treatment. To decrease absorbed dose to the heart and lungs a technique known as deep inspiration breath-hold (DIBH) can be used during radiotherapy [1–3]. With DIBH, patients are (using audial guidance with or without visual feedback), asked to take a deep breath and hold it during irradiation [4–6]. When the lungs are inflated the distance between the target (breast and lymph nodes) and heart is increased [7,8] and a lower fraction of the lung volume is irradiated [9].

The respiratory motion signal can be used to automatically trigger imaging and treatment [10]. A gating window (typically 2-5 mm) is set individually for each patient based on their particular respiratory motion during free breathing and DIBH. The respiratory motion signal is acquired at a predefined gating area, usually the xiphoid process [11]. Nevertheless, due to change in patient breathing pattern, room ambience and tissue swelling etc., changing the position of the gating area can be required. A study by Lutz et al. indicate a better breath-hold control with the gating area closer to the target at the body of the sternum instead of a position at the level of the xiphoid process [12]. Skyttä et al. have also showed that a gating area at a position closer to the target, 4 cm cranially instead of 4 cm caudally from the xiphoid process, can reduce the errors in the actual breath-hold level measured with lateral kV images [13]. Rong et al. found that the target position accuracy could be improved with a second gating area at the target breast as a supplement to a gating area at the xiphoid process [14]. These studies indicate a difference between the breath-holds measured at the xiphoid process and the target breast, but the feasibility of moving the gating area during treatment is not obvious.

In this study we used an optical surface scanning system to investigate the feasibility of moving the gating area during the course of treatment from the area above the xiphoid process or at the right breast to the target breast. The feasibility was evaluated using the *reproducibility* and *stability* of the breath-holds measured at the target breast, which was measured simultaneously with the breath-holds at

the gating area. Further, the inter-fraction baseline variation dependency with patient obesity measure (body index) was investigated.

2. Material & Methods

2.1 Patients

A total of 276 left-sided breast cancer patients, were treated with DIBH radiotherapy in the period July 2014 to June 2015at our department. Fourteen of these patients were not included in the study due to missing data (n = 3), gating area placement not in accordance with current study (n = 6), gating area moved during treatment (n = 3), gating window changed during treatment (n = 2). Patient characteristics of included patients are summarized in Table 1. The *stability* and *reproducibility* were estimated for 194 lumpectomy patients, as 16 lumpectomy patients were excluded due to different technical issues. The baseline variation dependency with patient obesity was evaluated for all patients (52 mastectomy and 210 lumpectomy patients).

2.2 Respiratory Motion Monitoring

The respiratory motion was monitored using the optical surface scanning system Sentinel™ (in CT room) and Catalyst™ (in treatment room) (C-RAD positioning AB, Uppsala, Sweden), and patients were audio-visually guided to hold their breath within a certain gating window (Figure 1). If the actual baseline deviated more than 2 mm from the reference baseline it was recalculated, and the gating window adjusted accordingly to maintain the planned breath-hold level. Recalculation of baseline was not performed during treatment (after patient setup). The respiratory motion signal was acquired using a circular gating area with a radius 2 cm. The gating area only detected differences in the vertical direction, and was spatially fixed in the lateral and longitudinal directions. Preferably, the area above the xiphoid process was used as gating area (Figure 1A). If the signal reception was inadequate, the gating area was moved slightly laterally and caudally. This is still a xiphoid-near gating area and regarded as ‘xiphoid’ in this study. If both lateral positions were not adequate the gating area was set at the right (healthy) breast (n = 25). The width of the gating window was

set between 1.5 (preferably 2) and 4.5 mm (median 2.5 mm). For lumpectomy patients an additional gating area (passive gating area) was placed at the left breast to acquire two respiratory motion signals simultaneously. The gating area at the left breast was used only for post treatment analyses. We did not use a passive gating area for mastectomy patients due to the use of tissue equivalent material (bolus) placed on the target breast, which deteriorated the signal.

Table 1: Summary of included patients.

Patient characteristics	Total
No. of patients	262
Fractionation scheme	
- Normofractionated (50 Gy/25 fractions)	132
- Hypofractionated (40 Gy/15 fractions)	130
No Boost	227
Boost scheme	35
- 10 Gy/5 fractions	27
- 16 Gy/8 fractions	8
Gating area at xiphoid process	237
- Passive gating area at left breast	171
- No passive gating area	63
Gating area at right breast	25
- Passive gating area at left breast	23
- No passive gating area	2
Mean age [y]	61 [34 to 84]

2.3 Data processing

A total of 10598 surface motion signals (a motion file is saved every time the baseline is recalculated) acquired after daily imaging (15-33fractions, 262 patients), were analysed using MATLAB R2015a (The MathWorks, Inc., Natwick, USA). The baseline, defined as the minimum signal value for the first 10 seconds, of the respiratory motion signal was extracted (Figure 1C). The inter-fraction baseline variation was evaluated using the standard deviation of the respiratory motion baseline measured at the gating area. The respiratory motion

signal values at the gating area (xiphoid process or right breast) were extracted when a breath-hold was within the gating window. The corresponding values where extracted for the respiratory motion signal measured at the passive gating area (left breast).

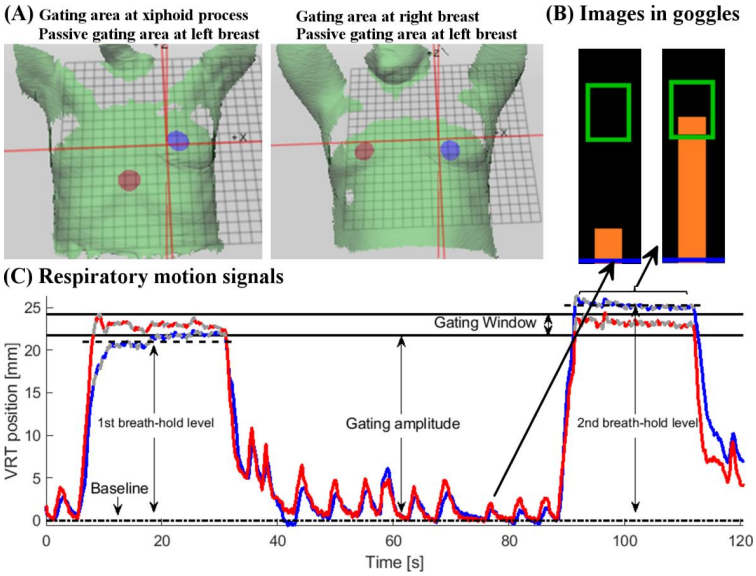

Figure 1: Illustration of the gating procedure. **A**: Example of placement of the gating area (red) and passive gating area (blue). **B**: The image in the video goggles at free breathing and at breath-hold. **C**: The respiratory motion signal measured at the gating area (red) and passive gating area (blue) during one fraction, the baseline has been subtracted. The breath-hold level is the average signal value of a given breath-hold. The respiratory motion signal at the passive gating area was scaled so the mean value within the gating window for all breath-holds was equal to the corresponding mean value for the signal at the gating area.

Body index was calculated as the volume of the CT based body outline divided by the scan length, and used for estimation of patient obesity as weight and height data was not available.

The *stability* of the breath-holds was defined as the standard deviation of the differences between the respiratory motion signal values measured at the gating area and at the left breast. *Intra-fraction reproducibility* of the breath-holds measured at the left breast was defined according to Cerviño et al. [5] as the

maximum difference between different breath-hold levels occurring within the same treatment fraction. *Inter-fraction reproducibility* of the breath-holds measured at the left breast was defined as the maximum difference between different breath-hold levels occurring within the whole treatment course for a given patient. The intra- and inter-fraction reproducibility were considered clinically acceptable if below or equal to 5 mm, and were considered poor above 5 mm.

2.4 Statistics

Linear regression analysis was used to assess the effect of the body index on the standard deviation of the baseline of the respiratory motion signal measured at the gating area. Wilcoxon signed-rank test was used to test if the right breast mainly was used as alternative gating area for patients with high body index, and to see whether the gating amplitude was larger when the xiphoid process was used as gating area. The F-test was used to test for differences between the variation of the baseline for the mastectomy and lumpectomy patients. Significance level of the hypothesis tests was set to $\alpha = 5\%$.

3. Results

An acceptable inter-fraction reproducibility (≤ 5mm) was seen in 44% of the patients (Figure 2), ranging from 2 to 28 mm and with a median value of 5.7 mm. The maximum intra-fraction reproducibility observed for each patient was acceptable (≤ 5mm) in 82% of the patients, and ranged from 0.4 to 18 mm with a median value of 2.7 mm. The intra-fraction reproducibility was acceptable in 91% of the treatment fractions. For the patients with high and low body index (≤ 50^{th} percentile) the inter-fraction reproducibility was acceptable in 35% and 53%, respectively, while the intra-fraction reproducibility was acceptable in 76% and 88%, respectively (Figure 2). The mean breath-hold stability of each individual patient was better than 2 mm for all patients. Examples of acceptable and poor inter- and intra-fraction reproducibility are shown in Figure 3.

Linear regression analysis showed that standard deviation of the respiratory motion baseline increased significantly with the body index (Table 2A).The

standard deviation of the baseline was significantly higher for the mastectomy patients (Figure 4 and Table 2D). The body index was significantly higher for the patients where the right breast was used as gating area instead of the xiphoid process (Table 2B). The gating amplitude was significantly larger for the patients with the gating area at xiphoid process compared to the right breast (Table 2C).

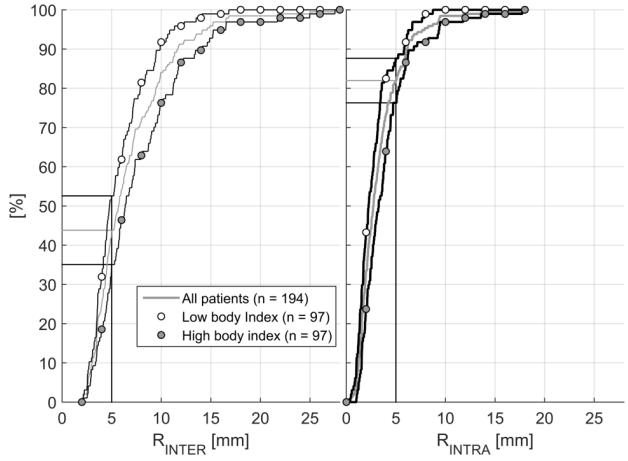

Figure 2: Cumulative plot of inter-fraction reproducibility (R_{inter}) and the maximum intra-fraction reproducibility observed for each patient (R_{intra}), of the breath-holds measured at the target breast. Plotted for all patients, patients with low body index (≤ 50th percentile) and patients with high body index (>50th percentile). The percentages of patients that have an acceptable intra- or inter-fraction reproducibility (≤ 5 mm) are marked with a horizontal line.

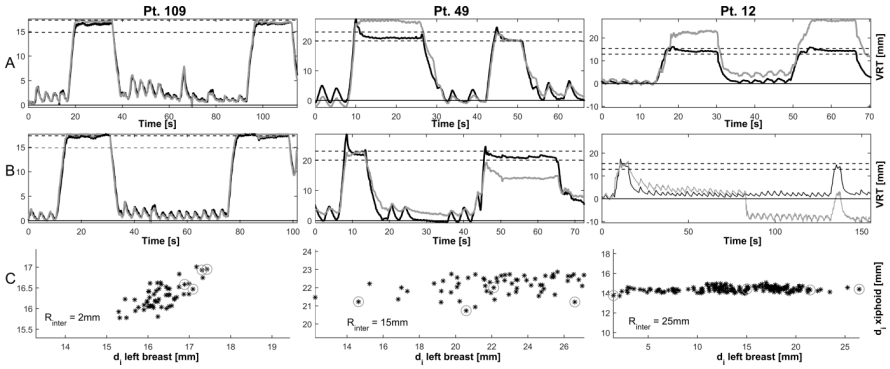

Figure 3: Examples of good intra- and inter-fraction reproducibility (Patient 109) and poor intra- and inter-fraction reproducibility (Patient 49 and 12). A & B: The respiratory motion signal measured at the left breast (grey) and xiphoid process (black) at two different fractions. C: The average breath-hold level d_i measured at the left breast and xiphoid process. Each observation represents one breath-hold. The breath-holds from row A and B is highlighted with a grey circle in row C. Note the large differences in breath-hold levels for patients 12, which are caused by a baseline shift in the respiratory motion signal measured at the target breast without a shift in the signal at the gating area.

Table 2: Hypothesis test used with corresponding p-value and the median together with its 95% confidence interval.

	Hypothesis	Test	p-value	Median (95% CI)
A	H_0:The model has no explanatory power H_1: Body index has an effect on baseline SD	Linear regression analysis	≤0.0001	
B	H_0:BI_{RB}-$BI_{XP} = 0$ H_1: $BI_{RB} > BI_{XP}$	Wilcoxon signed-rank test, one-sided	≤0.0001	XP: 597 (583-612) cm^2 RB: 731 (676-785) cm^2
C	H_0: $\|DIBH\|_{RB}$-$\|DIBH\|_{XP}$=0 H_1: $\|DIBH\|_{XP} > \|DIBH\|_{RB}$	Wilcoxon signed-rank test, one-sided	≤0.0001	XP: 13 (12-13) mm RB: 10 (9-12) mm
D	H_0: $var(B)_{mast}$=$var(B)_{lump}$ H_1: $var(B)_{mast}$>$var(B)_{lump}$	Two-sample F-test for equal variances, one-sided	≤0.0001	

BI: Body index, XP: Xiphoid process, RB: Right breast, |DIBH|: gating amplitude (Figure 1C). $Var(B)_{mast}$ & $var(B)_{lump}$: Variance of baseline for mastectomy and lumpectomy patients for whole treatment course, respectively.

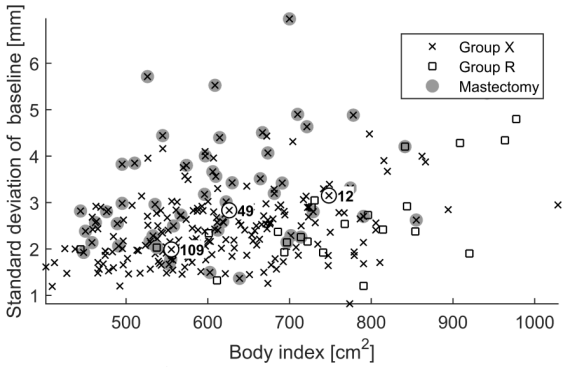

Figure 4: Standard deviation of the respiratory motion baseline through the treatment course for the different patients. The respiratory motion signal was measured at the xiphoid process (Group X) or the right breast (Group R). The three patients highlighted with a black circle are the patients from Figure 3.

4. Discussion

The primary aim of this study was to look into the feasibility of shifting the gating area from the area above the xiphoid process to the target breast during the treatment course. The gating area was for 25 out of the 262 patients placed at the right breast in the CT room as xiphoid-near gating area was not possible. Hence, it can seem contradictory that the effect of moving the gating area to the target breast during treatment was investigated. However, there is a cardinal difference between spatially moving the gating area during the treatment course, and placing it at a given position to begin with. In the latter an improved reproducibility can be expected due to visual guidance.

In our study, shifting of the gating area required an acceptable intra- and inter-fraction reproducibility ($\leq$ 5mm) and a good stability (below 2 mm) of the breath-holds at the target breast. For the majority of patients (109 out of 194) there was a poor inter-fraction reproducibility of the breath-holds at the target breast, while the intra-fraction reproducibility was acceptable in the majority of patients (159 out of 194). The stability of the breath-holds at the left breast was good for all patients (below 2 mm). In the current study a threshold for an acceptable inter-fraction reproducibility was set to 5 mm, although data shows

that even with a threshold of 10 mm only 86% of the patients would have an acceptable inter-fraction reproducibility (Figure 2).

Since the patients were visually guided by the respiratory motion signal at the gating area and no guidance was used for the passive gating area at the target breast, less stability may be expected. This is a cardinal limitation of this study. Both signals can be influenced by inter- and intra-fractional patient position variations and differences in the curvature of the patient surface around the gating areas. However, rotations around the patient's longitudinal axis are likely to influence the gating areas on the breasts more than the gating area at the xiphoid process. Changes in the position of the patient in the longitudinal and transversal direction might influence the two gating areas differently as the patient curvature around the gating areas is different. Furthermore, during breathing motion or from fraction to fraction (due to setup differences) the breast can move in and out of the gating area, which can give rise to differences in the respiratory motion signal. This is because the gating area is fixed relative to the coordinate system of the linear accelerator and not to the patient surface. For the patients where a baseline shift was only seen in the respiratory motion signal measured at the left breast, the intra-fraction reproducibility could be improved in a clinical situation by recalculating the baseline. However, in our clinic it is in general not advised to correct for baseline shifts during treatment after the initial image guided patient setup. The patient is instead instructed to relax her breathing in order to re-establish the baseline.

In this study we did not correlate the respiratory motion signal with the inner anatomy (chest wall etc.), so basically we do not know which signal best correlates with the position of the target breast. The poor inter-fraction reproducibility could be a result of the anatomy of the breast being less appropriate as gating area compared to the area above the xiphoid process. That the gating area above the xiphoid process is more appropriate is supported by other studies showing a good correspondence between chest-wall position and the xiphoid process [13,15]. Lutz et al. also found a good correspondence with mean setup errors of the chest-wall below 5 mm in 97.8% of the recorded fields,

measured using continuous portal imaging during DIBH radiotherapy with a gating area near the xiphoid process [12]. The maximum intra-fraction reproducibility of 18 mm could in the worst case mean that an 18 mm shift in the target breast occurs from one breath-hold to another without being detected by the motion at the gating area (right breast/xiphoid). This could potentially lead to a corresponding shift in the delivered dose distribution with respect to the target, which could compromise target coverage and increase dose to the organs at risk. However, the shift is most likely a result of the breast being less appropriate as gating area.

The right breast was more often used at gating area for the patients with high body index. This is probably related to the patient's abdomen blocking the path between the area at the xiphoid process and the camera of the optical surface scanning system. Schönecker et al. and Koivumäki et al. used the same optical surface scanning system for DIBH radiotherapy for 13 and 15 breast cancer patients, respectively [10,16], and a gating area near the xiphoid process, but did not report having any difficulties acquiring signal. Schönecker et al. however did express a concern about a potential blocking issue. A simple solution could be increasing the angle of the breast board or using a three camera solution. If these solutions are not feasible we would on the basis of this study and the previous studies from Lutz et al. and Skyttä et al. [12,13] recommend to move the gating area cranially towards the body of the sternum as a second option and only choose the target breast (if no bolus is used) or the contralateral breast as a last resort. Choosing the breast as gating area may require that both setup and treatment field imaging is implemented in the daily clinical routine.

The standard deviation of the baseline increased significantly with the body index. This is in agreement with our experience that it is more challenging to setup obese patients, resulting in increased baseline variation. The sub-group of patients with a high body index also had a lower percentage of acceptable intra- and intra-fraction reproducibility ($\leq$ 5mm). The baseline variation could possibly be lowered by correcting for any thorax rotation at setup for example by using an optical surface scanning system for positioning prior to treatment. The variation of

the baseline was in general higher for mastectomy patients. This can be caused by bolus used above the cicatrise region in the mastectomy patients. The uncertainty in the manual placement of the bolus can potentially result in the bolus being inside the gating area in some fractions and outside in other fractions. The respiratory motion baseline at the target breast at the end of the treatment course did not have a significantly larger value compared to the beginning of the treatment course (data not shown). This implies that no swelling of the breast occurs over the treatment course, although the noise level may hide small changes.

In conclusion, the study showed a large inter-fraction variation of the breath-holds acquired at the target (left) breast for the majority of patients, which implies that the gating area in general should not be moved from the xiphoid process or the right breast to the target breast during the course of treatment. Obese patients (with high body index) showed larger inter-fraction variation of the respiratory motion baseline, indicating larger setup errors for these patients.

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6. Declaration of interest

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